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THE

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OF THE MEDICAL SCIENCES

JUNE, 1925

ORIGINAL ARTICLES.

EFFECT OF PREMATURE DOGMATIZATION IN MEDICAL SCIENCE.

ILLUSTRATED IN THE FIELD OF ANAPHYLAXIS AND IMMUNITY.

BY W. H. MANWARING, M.D.

PROFESSOR OF BACTERIOLOGY AND EXPERIMENTAL PATHOLOGY, STANFORD UNIVERSITY SCHOOL OF MEDICINE, STANFORD UNIVERSITY, CALIFORNIA.

INTUITIVE dogmatization from inadequate data not infrequently plays a prominent role in medical science and is a major handicap in research. In no field are its effects more evident than in the field of anaphylaxis and immunity.

The success of Jennerian vaccination supplemented by statistics in other diseases led to the early intuitive generalization that artificial inoculation and natural infection invariably leave behind them an increased resistance or acquired immunity to reinfection, that physicians have but to find suitable vaccines to control all infectious processes. Although this was never more than a subconscious dogma in scientific medicine, it nevertheless dominated medical thought during the nineteenth century, was the basis of interpretation for immunological phenomena, and made possible lucrative exploitation of prophylactic and therapeutic vaccines in spite of inadequate evidence in their support. The dogma so biased clinicians that failure of a vaccine was not interpreted as evidence against the dogma, but merely as an indication that the proper vaccine had not yet been found.

The dogma also blinded non-clinical workers. Flagrant contradictions to the basal assumption were repeatedly overlooked or

ignored by laboratory men, or discarded by them as of no significance, presumably due to idiosyncrasies or to experimental errors. It would be of interest to collect from the literature of the nineteenth century the numerous examples of the blinding effect of this dogma on observational science. The most striking example thus far brought to light is that of Magendie, who, in 1839, regarded as of little or no significance acquired protein hypersensitiveness in his laboratory animals, protocols now seen to be practically identical with those for which Richet, seventy-four years later, was awarded the Nobel Prize. During the last two decades of the nineteenth century scores of similar protocols were ignored or discarded by the foremost research workers of both hemispheres, humble tribute to the narcotizing effect of intuitive dogma.

With Behring's observation in 1890 that sera of animals immunized against diphtheria toxin have antitoxic properties sufficient to control diphtheria in the other animals, there was the further intuitive generalization that the essential defense against all infections is located in the blood stream, that foreign serum is capable of harmonious coöperation with the normal defenses of the human body, and that physicians have but to find suitable sera to control all infectious diseases. This intuitive dogma made possible lucrative exploitation of alleged prophylactic and curative sera in spite of inadequate evidence in their support, and so blinded clinicians that failure of a serum was not interpreted as evidence against the dogma, but merely as an indication that the proper serum had not yet been found.

The dogma also dominated theoretical research. For three decades immunology developed almost solely along serological lines, a juggling of shifting hypotheses to fit the major premise that all immunological phenomena are due to serum changes, ignoring the possibility that essential immunity factors might be located in the fixed tissues. That fixed tissues often play a dominant role in immunity is now generally realized. Transfusion of practically the total blood volume of an immune donor will not always confer immunity upon the recipient.[1]

With the observations of Richet and of Arthus in 1902, that animals injected with foreign protein often become hypersensitive, reinjection causing violent local or systemic reactions, there was the further intuitive dogmatization that all infections leave behind them a subnormal resistance to reinfection superimposed upon the assumed immunity factors, that vaccines and sera are of use only in those diseases in which the immunity factors can be made to dominate. This basal conception of two antagonistic mechanisms, a superposition of anaphylactic and immunity factors, is the preva-

[1] Manwaring, W. H., and Bronfenbrenner, J.: Intraperitoneal Lysis of Tubercle Bacilli, Jour. Exper. Med., 1913, **18**, 601.

lent current conception of the relationship between anaphylaxis and immunity.

Recent experiments lead one to question the validity of this conception, to wonder if it in turn is not an intuitive dogma, seriously handicapping theoretical and practical medicine. Opie,[2] for example, finds that local anaphylaxis serves the useful purpose of preventing the absorption of specific foreign protein from the site of injection, thus protecting more important internal parts. A paradox of an apparently subnormal local resistance playing a purposeful role in systemic immunity.

It would not take an oriental imagination to picture all known anaphylactic phenomena in this light. The vascular reactions on which the Arthus phenomenon depends could thus be looked upon as purposeful physiological reactions designed to prevent the absorption of unwelcome proteins, a source of serious danger to the individual only under the artificial conditions of current anaphylactic research, intravenous injection of overwhelming doses of specific foreign protein. The characteristic anaphylactic bronchial reactions could be pictured as purposeful physiological defenses preventing the entrance of unwelcome agents into the pulmonary alveoli, a source of danger only on massive intravenous injections, throwing all parts of the bronchial tree into simultaneous constriction. The intestinal and esophageal reactions, as purposeful mechanisms for the rapid removal of unwelcome gastro-intestinal contents. The hepatic reactions, as purposeful adaptations for the rapid destruction or elimination of unwelcome products from the blood stream.

That this conception of the fundamental relation between anaphylaxis and immunity is more than a mere poetic conception, is indicated by the fact that, so far as tested, the immunity reactions of isolated fixed-tissues are identical with the so-called anaphylactic reactions. Typical anaphylactic responses are given by immune tissues on perfusion with normal blood plus specific foreign protein.[3] This conception of the essential identity of anaphylaxis and immunity would render obsolete the entire current nomenclature of anaphylaxis.

Study of the anaphylactic responses of fixed tissues, therefore, is of vital interest to theoretical and practical medicine, and may furnish facts on which the immuno-therapy of the future may largely depend.

[2] The Relation of Local Sensitization to Immunity, Jour. Immunol., 1924, **9**, 259.

[3] Manwaring, W. H. and Kusama, Y.: Analysis of Anaphylactic and Immune Reactions by Means of the Isolated Guinea-pig Lungs, Jour. Immunol., 1917, **2**, 157.

IS OUR KNOWLEDGE OF PNEUMONIA SUFFICIENT TO EXPLAIN ITS ENDEMICITY AND OCCASIONAL EPIDEMICITY?*

By A. C. Abbott,

DIRECTOR SCHOOL OF HYGIENE, PUBLIC HEALTH, UNIVERSITY OF PENNSYLVANIA.

As I view the current problem of pneumonia our knowledge of that disease is, in a number of important particulars, so defective that definite conclusions are difficult, if not impossible. It is with the intention of indicating what I regard as some of these deficiencies and of offering certain suggestions for further investigation, that I accept your kind invitation to take part in this discussion.

If the views that I express are not altogether in harmony with those commonly held, it is because I am convinced that the studies thus far made of pneumonia have not been sufficiently comprehensive. While they have shed much light upon the character of the pulmonary lesions and have offered many helpful suggestions as to the causation of those local conditions, I cannot avoid the opinion that they have done but little in clarifying the larger problem of the origin of pneumonia as a constitutional and probably transmissible disease; and insofar as they enable a full and complete discussion of either the epidemiology or the endemicity of pneumonia, I am sure you will agree with me that they are insufficient and often may be misleading.

Such reliable data as are available upon the strictly epidemic features of this disease have come, in the main, from studies upon pneumonia as it has occurred and spread in more or less circumscribed localities—as in army and contract camps, in hospital wards, asylums and the like; though I am aware it has at times taken a much wider scope. In these instances the designation epidemic appears to be entirely appropriate. But when we view the disease as it occurs among the population at large, we get a very different impression. If its occurrence be expressed graphically the resulting curves suggest more the irregular fluctuations in an ubiquitous, endemic disease than of epidemic outbreaks. It is my belief therefore that such studies as may shed light upon the endemicity of pneumonia may be more enlightening than those directed to its epidemicity.

Almost the first difficulty encountered in such a study is that we do not know precisely what is meant by the term, "Pneumonia," as the word appears in the majority of available statistical records. Is the word used generically, that is, to include all acute inflammations of the lungs? Does it mean the typical lobar pneu-

* Read before the Philadelphia County Medical Society, January 28, 1925.

monia or the broncho-pneumonia? Or does it mean those inflammatory conditions of the lung substance, often fatal, that follow the invasion of the lungs by microbes not ordinarily associated in our minds with the disease pneumonia? Are we to regard these various lung conditions as disease entities of manifold origins or only as secondary processes engrafted upon a specific primary infective process the existence, nature and exciting cause of which are as yet unknown?

From the present knowledge and records none of these questions can be answered satisfactorily. The result is that we cannot approach an analysis of this subject with the same degree of confidence as would be the case were we discussing such definite phenomena, as are manifested by the notoriously epidemic maladies, cholera, typhoid, plague and so forth.

From this I think you will appreciate that at the very threshold of our inquiry an obstacle presents that may render subsequent steps and conclusions uncertain and fallacious.

We learned much and should have been put securely on our guard by the experiences of the recent tragic pandemic of influenza. I believe I am well within safe limits when I say that a comparatively small number of the fatal pneumonias consequent upon influenza were of the uncomplicated croupous or lobar type—yet they were pneumonia—inflammation of the lung—and often proved fatal and apparently transmissible.

Before one is in a position to speak confidently on the origin of pneumonia it is imperative that a classification of these various manifestations be made. As the matter now stands almost the only deduction that one can make from the published figures is, vague as it may seem, that some, as yet unknown factor predisposes from time to time varying numbers of individuals to inflammation of the thoracic viscera; and that in certain instances these infections group themselves in such a manner, pathologically and clinically, as to suggest a common, specific, exciting cause, while in others they do not.

That the typical frank, lobar or fibrinous pneumonia—the most dramatic picture in clinical medicine— is a definite disease entity no one can at this time doubt—but by no means all pneumonias are of this type and hence a difficulty.

I do not find the task of interpretation much lightened even by a consideration of true lobar pneumonia alone; for when we review the data that we have on that disease we cannot but exclaim: if we are in possession of all the facts concerning the specific etiology of this disease, why is it not possible to do more in either its prevention or its cure, or both? In spite of all that has been done, and well done, and all that we think we know of this disease, the mortality reports show a steady persistence of pneumonia in practically all parts of the country.

I am aware that the doubt here implied as to the sufficiency of our knowledge, is treading on rather sacred ground, yet I cannot avoid the impulse to risk it.

It would be superfluous to detain you with a recital of the prevailing view of the relationship between lobar pneumonia and one or another of the several varieties of pneumococcus always present in the diseased lung. Because of this regular association, the opinion is very general that pneumococcus is the one and only vital factor concerned in true lobar pneumonia. This view is as fixed in the minds of many as was at one time the view that the so-called hog cholera bacillus, always present in the characteristic lesions of that disease, was the cause of hog cholera—yet time has shown that throughout all the careful experimental work on hog cholera we were, for the most part, unconsciously dealing with at least two exciting factors: one, quite obvious, easily recognizable, and readily lending itself to experimental study, the hog cholera bacillus—the other, obscure, evasive, invisible, but apparently ever present, a filterable or ultra virus. The one, the latter, the real cause of the disease; the other, the former, only a regular accompaniment. As a result, years of labor and reams of publications upon hog cholera are today but of historic interest.

Let us consider for a moment some of the work that is based on the belief in an etiological relationship between pneumococcus and pneumonia and forget all else for the time being.

We find that with every case of classical, clinical, lobar pneumonia, pneumococcus of one type or another is always present. There is no room for doubt that it is the agent accountable for the pathological lesions of the lung that characterize the disease. We do not find, however, that recovery from a pneumococcus pneumonia confers immunity from a second invasion, either by the homologous type of pneumococcus or a primary invasion by one or another of the related types. In fact, a primary attack seems in some instances to predispose to subsequent attacks. We find that by following customary immunologic methods serum may be obtained from experimental animals that may exhibit more or less protection to other animals from general infection by the homologous pneumococcus strain. But on man, we also find that the homologous serum obtained from the experimental animal has, as a rule, rather a disappointing influence on pneumonia.

As a result of all this one cannot avoid the suspicion that the problem of pneumonia in man is being approached in a too restricted way. Perhaps were more of the effort directed to the prodromes of the disease pneumonia and less to the local lesion and the intimate peculiarities of the pneumococcus accountable for the local lesions, something of greater value to a full understanding of the origin of the disease might result. In making this comment I have no intention of belittling the value of the current experimental activities.

I wish only to convey the idea that I regard their scope as too circumscribed and I believe the work based on the assumption that pneumococcus and pneumococcus alone is the cause of pneumonia has gone far enough to justify the suspicion that some other agent, as yet not identified, may be concerned primarily in exciting the disease; in preparing the way for the lung developments.

This should not be considered as either destructive or retrograde. I have already mentioned the hog cholera experience—that of influenza may properly be recalled to our minds. For years after Pfeiffer introduced us to the organism that bears his name, opinion was pretty well centered upon the Pfeiffer bacillus as the cause of influenza. It was always present in true cases—still is for that matter; it appeared early in the disease and persisted late into convalescence. Experiments demonstrated that one of its characteristics was the elaboration of an intoxicant which when injected into lower animals called forth signs and symptoms strikingly like those seen in man suffering from the disease. It seemed to many that all the postulates needed to establish a causal relationship of that organism to influenza had been reasonably fulfilled—yet we now learn, through the work of Olitzky and Gates— that during the first thirty-six hours of influenza—and not after that time—there is to be found in the exudates from that disease, an organism hitherto unrecognized—differing in many important particulars from the common run of bacteria; which organism they believe to be the primary invader in influenza; playing the role during its early sojourn in the tissues of preparing the way for the later invasion and activities of the Pfeiffer bacillus and the other organisms so commonly seen in influenza.

If one might be permitted to speculate, it seems more than reasonable to suspect that this "preparer" of Olitzky and Gates had been in the tissues for a longer time than thirty-six hours; its invasion probably antedating its disappearance and the advent of recognizable symptoms by many hours; an interval that we may call the incubative time. Also it may be conceived that, as in the case of measles, this primary period, before either disease can be recognized clinically, may be that of highest contagiosity. This view would at once account for the difficulty, yes the impossibility, of preventing dissemination.

I am not unmindful of the impressive experiments of Cecil and Blake on artificially induced pneumonia in monkeys, yet I cannot shake from my mind that we may have gone sufficiently far on the assumption that pneumococcus is the one and only organism concerned in originating the disease pneumonia as we see it in man; and that the lesions of the lungs, vitally important though they be, comprise all that is of moment in the development of this ubiquitous malady.

I believe the time is ripe for the study of pneumonia to be begun

from another viewpoint; a viewpoint that does not regard the local pulmonary conditions as the disease, but rather as a pathological phenomenon engrafted upon a condition that had been excited and prepared by a living germ as yet unidentified.

It is pretty generally agreed that the discovery of the exciting cause of a disease is the first step toward its ultimate eradication. One is forced by this dogma to exclaim: if pneumococcus is the exciting cause of the disease pneumonia why then has so little progress been made in lessening the incidence of pneumonia? Have we in the pneumococcus the real cause of pneumonia or is it only the organism responsible for an outstanding lesion peculiar to the disease? I do not anticipate that this suspicion of a possible dual etiology for pneumonia will be the cause of much astonishment. All through the work on this malady, both clinical and experimental, one frequently encounters the suspicion of the activities of some "unknown factor," some, "determining influence," some, "predisposing cause," and so forth, and it is significant that these expressions convey to me at least, the impression that there is now and then in the minds of those using them not a predisposing influence as the expression ordinarily implies, but rather something vital, more direct, more specific, something, possibly, that is operative either coincident with or anterior to the activities of the pneumococcus, or the streptococcus or whatever other organisms that may be concerned in the pulmonary changes. If these speculations be worthy of consideration it is not inconceivable that the origin of the real disease, pneumonia, not only antedates the lung changes, but may coincide with the invasion of the body by a totally different parasite from those commonly and easily found in the various pulmonic phenomena that accompany the disease later on. At one time these secondary local lesions may be those of the true fibrinous, lobar inflammation from which lobar pneumonia takes its name; and which are due to the activities of pneumococci; at other times the engrafted lung lesions may be of the bronchial type, commonly following influenza, and arise from the invasion by one or another variety of streptococci; at still others, from one or more diverse organisms singly or together, that are not usually associated in our minds with the disease pneumonia. Sometimes sharp etiological distinctions for the lung lesions are difficult to make. Whether these doubts upon the sufficiency of our knowledge of the real cause of pneumonia are worth more than passing notice cannot be decided, as they are not based upon any convincing experimental data; but even so, it is highly desirable that experimental inquiry be directed to something other than the lung conditions seen in the various manifestations of the disease we call pneumonia.

From the vast amount of work that has been done on this puzzling disease, what is it possible for us to glean that is of value in enlightening us upon the reasons for its endemicity and its occasional epidemicity? From my standpoint, very little.

There are no good grounds for doubting that the organisms accountable for the characteristic pathology of pneumonia gain access to the lungs by way of either the mouth or nose, and should the future reveal the presence of some additional organism as yet unknown that may serve to prepare the way for the commonly present pneumococci and streptococci—it may be predicted that that questionable organism will be found to have the same portal of entry. In any event and obviously the transmission of the disease is to be prevented by making impossible the transference of materials from the oral and nasal cavities of the sick to those of others in the neighborhood.

I have no doubt that those of you who have studied in detail the immunologic reactions of the various types of pneumococcus will be astonished when I say I am by no means convinced that the pneumococcus commonly present in the mouth cavity as a commensal is so fixed in its innocent qualities that it may be dismissed with little or no consideration. Nor am I of the opinion that we are as yet in a position to conclude that, under as yet unknown influences, it may not acquire dangerous characters, all immunologic arguments to the contrary, notwithstanding; especially if coincident with or antedating its entry into the lung, the resistance of the tissues has been reduced through the activities of some other as yet unidentified microbe. I am quite certain that this suggestion will be received with many reservations, because of the fixity and almost universality of the belief in the nontransmutability of the various types of pneumococcus. Remember please that the types of pneumococci are not immutable species—they are but varieties of one and the same original species; they have evolved presumably through environmental influences which are as yet unknown to us; and remember too that the characters by which these various types are distinguished the one from the other are not structural, that is morphologic, but are functional, that is physiologic, a distinction of very great moment to an understanding of their relationship.

If, through environment with which we are not acquainted, these four or five types, with their countless subvariations can evolve, is it inconceivable that by analogous influences the usually harmless commensal variety may acquire dangerous characters; either through changes within itself or through association with some other organism, either symbiotically or in sequence? Taking the matter in the reverse order—it is a common observation that the highly virulent pneumococci present in the lungs during pneumonia frequently become less and less virulent as convalescence proceeds until they often become almost devoid of that property; especially when they reach the upper air passages. We see then that under natural surroundings virulence is variable and by no means a fixed quality. It is not at all an uncommon observation that persons

in attendance on patients ill of pneumonia often have in the upper air passages pneumococci of the same type as that in the lungs of the patient; yet the attendants, with a few exceptions, escape pneumonia; and what is of equal interest, the virulent pneumococci usually disappear completely or they gradually assume the pathogenic characters of the lowly virulent or harmless type.

Whether the various accepted types of pneumococci persist as distinctly pathogenic potentials or not, the practical fact remains that they are found in the normal mouth or in the diseased body only; the human being must therefore be regarded as the transmitting agent, the focus of possible danger.

At first glance all this seems to simplify the matter very much—but does it? Not to my mind. Would we be justified, in view of what we know of the ubiquity of pneumococci among normal human beings, in separating from their fellows all persons known to harbor this organism, or, accepting the type doctrine, could we identify and isolate all persons known to harbor those types commonly present in the pneumonic lung—or again would it, in the present state of our knowledge, be advisable to do so?

If it is conceivable that a systemic condition antedates the lung expressions seen in a fully developed case of pneumonia, and is caused by a vital agent as yet undiscovered, may we not have at least a speculative explanation for the transmission and ever presence of the malady? Certainly no such explanation is afforded by studies thus far made on the assumption that pneumococcus causes the disease. May not the disease be most transmissible during its earliest, incubative stage, a time during which pneumonia as we know the disease is not in evidence? May we not from this viewpoint make at least one step toward a visualization of its endemicity, so important to an understanding of its epidemicity?

A very widespread opinion relating to the origin of pneumonia is that "common colds" (whatever that expression may comprehend) are often the precursor. So general indeed is this belief that one is forced to regard it as in part at least sound. What are the processes in common cold that may invite the advent of pneumonia? Up to the impressive experiments of Cecil and Blake—mentioned above—practically all of the experimental efforts to produce pneumonia in animals were predicated on the idea that in one manner or another the tissues of the lungs required to be prepared, before the pneumococci could proceed to elaborate the typical pneumonic lesion. Such preparation—the details need not be gone into here—aimed to interfere at various points in the lung with its normal function—either by shutting off lobules, plugging up bronchioles, or interfering with the local blood supply. Does not some or all of this occur in varying degree in common cold with the lung involvement that so often accompanies it?

What is it in the common cold that may function as the preparing

agent? Is it the ordinary organisms of the mouth or nose or those of the upper pharynx, or the filterable viruses to which attention has been directed in recent times, or is it the mechanical obstruction afforded by the accompanying catarrhal conditions? Possibly one, possibly all, but a certain reply cannot be made, for common colds have not as yet been subjected to the degree of experimental scrutiny that their importance demands.

Then again: if we consider measles; it is not measles alone that causes anxiety but the possible bronchopneumonia that so often follows it. During the past few years our notions of this disease have undergone some very radical revisions; as a result of which we now maintain that measles is at its highest stage of contagiosity before it can certainly be recognized as measles. That is to say—it is most contagious during the prodromes when it is often indistinguishable from a common cold. There does not exist the least evidence, either experimental or clinical, that measles and common colds are in any way related, yet in their earliest stages they are clinically indistinguishable from one another and in their later stages both often lead to inflammation of the thoracic viscera.

It is just such considerations as these that force me to wonder if we have derived through experimental effort thus far made, all that we should have for a correct interpretation of the various pneumonias, or for a sound understanding of the endemicity and occasional epidemicity of the disease.

From the foregoing considerations it is obviously impossible to make dogmatic statements concerning the important phases of this puzzling clinical and epidemological riddle.

After all the work that has been done on pneumonia there is scarcely an infective disease in which so little progress has been made in the way of its prevention.

It is not necessary for me to take your time in reciting that which is to be found in every modern text book on the general questions of transmission and prophylaxis. It is all based on the assumption that transmission is by way of matters ejected from the lungs, and that pneumococcus is the one and only factor to be considered. I have called that latter view into question with the hope that future investigations of pneumonia may depart from the beaten track and approach the problem through a new avenue.

Conclusions. The evidence does not justify the belief that the endemicity and occasional epidemicity of the disease pneumonia are due to the simple transference of one or another of the types of pneumococcus from the sick to the well.

The fact that recovery from pneumonia confers no appreciable immunity from subsequent invasions by the homologous type of pneumococcus (or by other types) justifies a question as to the etiological relationship of that organism to the disease pneumonia.

The occurrence of pneumonia as a result of the activities of

diverse organisms suggests the possibility that the lesions of the lungs are but secondary to an antecedent general or local condition brought about by some other as yet unidentified organism.

If the pulmonary lesions may be regarded as secondary developments, may not the spread of the disease be explained by the existence of some, as yet unknown, predisposing agent; and may not invasion and transmission occur before the disease is recognizable as pneumonia? This would explain the persistent, ubiquitous, high rate of morbidity as well as the occasional epidemic explosions.

THE SIMULATION OF ACUTE RESPIRATORY DISEASES BY SECONDARY LUNG TUMORS.

By Lloyd F. Craver, M.D.,
THE MEMORIAL HOSPITAL, NEW YORK CITY.

Malignant tumors hold today more interest than ever before, chiefly, probably, because of our increased therapeutic resources. One result of this increased interest is that these cases are now subjected to much more searching scrutiny, because with possession of several modes of treatment it becomes necessary to analyze each case individually, in order properly to judge which form of treatment is most suitable. For example, in dealing today with mammary cancer the surgeon feels that it is extremely important to know whether a slight cough, perhaps scarcely noticed by the patient, is a symptom of pulmonary metastasis, or whether a slight pain in the pelvis means bone metastasis. The writer has called attention[1] to the fact that for the early detection of pulmonary metastases physical signs, as well as the roentgen-ray, have a distinct value, and that in some instances physical signs are present before the appearance of symptoms, as stated by Roberts and Perkins,[2] and sometimes, apparently, before the roentgen-ray plate shows any abnormality. Manges[3] has also stressed the need for careful physical examination, instead of relying entirely on roentgen-ray examination.

In observing the course of cases of pulmonary metastasis several instances have come to our attention in which an acute respiratory disease has been closely simulated, in some cases even leading at first to errors in diagnosis. It is quite common for patients who have just developed evidence of pulmonary metastasis to say that they have recently caught cold, meaning usually that they have had a cough for two, three or four weeks, accompanied perhaps at the onset with malaise, chilliness and indefinite pains in the chest. Such cases are mentioned by Stokes,[4] Holt and Rattermann[5] and Robey.[6] Burt[7] cites a case of secondary spindle-cell sarcoma in

which, six months after removal of a tumor from the forearm, there was a sudden onset of pain in the right side of the chest and inability to get out of bed, followed in one week by shortness of breath, and in five weeks by death. Oliver[8] describes the sudden appearance of cough, pain in chest and dyspnea simultaneously with pains in extremities, heralding the coincident development of hypertrophic pulmonary osteoarthropathy and metastatic sarcoma of the lung.

There is, however, a distinct group of cases in which the onset and course of the pulmonary metastasis is much more stormy, so much so that, depending upon the symptom complex, a diagnosis of lobar or bronchopneumonia, acute pleurisy, empyema, tuberculous phthisis or acute miliary tuberculosis may be erroneously made. Acute miliary carcinosis or generalized pulmonary cancerous lymphangitis of the lungs in young subjects suffering from gastric carcinoma which may give no stomach symptoms has been described by Beger,[9] Bard,[10] Sternberg[11] and others. Empyema was simulated in a case of sarcoma (primary in lung ?) described by Rolleston and Trevor.[12] Marfan,[13] in 1893, in Charcot's *Traité de médecine,* under clinical forms of cancer of the lung, speaks of "cancer pleuropulmonaire aigu ou galopant," and cites the observations of Bucquoy, Duguet, Jaccoud, Hérard and Cornil in similar acute cases, but omits bibliographical references. Bard[14] quotes Marfan's description of the clinical picture as follows: "The disease, primary or secondary, develops with an astounding rapidity. In the midst of perfect health the patient begins to cough, exhibits an excessive dyspnea and dies in a month with progressive asphyxia; the diagnosis most frequently made is acute phthisis." Simulation of bronchitis, pneumonia, tuberculous phthisis or acute tuberculosis, and particularly caseous pneumonia affecting chiefly the base, as well as of pleural effusion or empyema is described by Roberts and Perkins.[2] Osler[15] gives brief mention to the "acute galloping pleuropneumonic form."

Several examples are found in the literature of simulation of pneumonia by secondary lung tumors. It may be that in many of these cases true pneumonia has been present in addition to the metastatic tumors. Burt[7] says: "As the tumor grows, reactive inflammation is apt to be set up, and in the lung the inflammation is usually catarrhal." Tyson and Fussell[16] speak of reactive pneumonia in tumors of lung as being the probable explanation of the time-honored symptom of prune-juice sputum, and also of the fever in these cases. On the other hand, Hellendall[17] thought that in his case the fibrinous pneumonia was an intercurrent affection, and prepared the soil for the growth of the metastases. In this case one and a half months following removal of a fibromyxosarcoma from the buttock a typical attack of pneumonia occurred, the temperature reaching 40.4° C., and a crisis occurring on the

tenth day. Following the crisis, however, the patient failed to recover, and showed symptoms and signs which were thought to be due to a postpneumonic phthisis, death ensuing one and a half months after onset of the pneumonia. Autopsy showed extensive secondary deposit of a tumor in the lungs identical in structure with that which had been removed from the buttock.

Others who have directed attention to symptoms suggestive of pneumonia in cases of rapid dissemination of secondary tumors in the lungs are Fowler and Godlee,[18] Martin,[19] Mix[20] and Sternberg.[11] Mix's patient had had a breast removed for carcinoma, and an operation for recurrence, yet a diagnosis of pneumonia was made, a blood culture was reported positive for pneumococcus and a great deal of laboratory investigation was made. To Mix the significant feature of the physical signs was that breath sounds were for the most part absent over the bases despite the presence of marked dulness. His comment seems justified: "When one approaches a patient who has had carcinoma of the breast, with a recurring nodule which has been removed by a surgeon, attention should at once be directed to possible carcinoma metastases. If you go into a field in which wheat has been sowed you expect to find wheat, and if you investigate a patient who has had carcinoma and who is sick, you will expect to find carcinoma metastasis. In such a case one ought not to look for Bright's disease, and make elaborate blood and urine chemical tests or immediately start making blood cultures; one should rather first examine the patient, and then having found out what the patient shows on physical examination, should at once direct investigative work toward these findings."

That acute pleurisy is often simulated by metastatic pulmonary growths was noted by Laennec[21] (cited by Unverricht,[22] who also quotes Trousseau as stating in his *Leçons de clinique médicale* that we possess no reliable symptom which puts us in a position to recognize the nature of the disease—pleural effusion). Dieulafoy[23] says: "Hemorrhagic pleurisy in cancer may arise quite suddenly, like acute pleurisy. . ." Montel and Hauvuy[24] have recently reported a case in which sarcoma of the thigh had been developing for four or five months without attracting attention, and in which suddenly dyspnea from a hemorrhagic purulent pleural effusion appeared and proved rapidly fatal.

Acute miliary tuberculosis was so closely simulated in a case of Zinn,[25] a pregnant woman, aged thirty-one years, with a chorioepithelioma, that an erroneous diagnosis was made. The clinical picture was at first dominated by marked dyspnea and cyanosis, together with hemoptysis and frequent vomiting. After a few days there was a sudden attack of extreme shortness of breath, cyanosis, fever (38.3° C.) and diffuse capillary bronchitis.

This paper deals only with secondary lung tumors, but it may not

be out of place to mention at this point that the acute onset also occurs in primary lung tumors, as stated by Marfan,[13] Pässler[26] and others.

Case Reports. The following cases have come under observation at Memorial Hospital since January, 1923. For the sake of brevity only the pertinent facts of each history are given.

CASE I.—A. McK., a white girl, aged seventeen years, suffered from periosteal osteogenic sarcoma of the lower end of the right femur, for which she had been admitted, October 29, 1923. She had had a series of roentgen-ray treatments.

On November 3, 1923, a roentgen-ray plate of the chest was negative for metastases.

On November 25, 1923, her temperature suddenly rose to 103° F., and there was marked shortness of breath, pain in the right side of the chest and some cough, but no expectoration. The house surgeon after examination of her chest said that he thought she had pneumonia. However, on the next day, November 26, the signs were those of a large pleural effusion on the right side, with a temperature of 104° F.; pulse, 144; repirations, 34. It was felt that the chances were that the illness was due to pulmonary metastasis with unusually severe reaction and pleural effusion. Thoracentesis obtained 14 ounces of blood-tinged fluid. There was a leukocytosis of 16,000. The next day, November 27, the temperature had fallen to 102° F., and she felt better.

On December 7, 1923, a roentgen-ray plate of the chest showed evidence of metastases.

The patient continued to have a slight fever, the temperature fluctuating between 98.5° and 101° F., finally subsiding by lysis after thirty-one days.

Examination of the lungs on December 13 showed the following: Flatness, with absent or greatly diminished breath sounds and tactile fremitus at right base posteriorly and laterally. Over right base anteriorly decreased breathing and crackling and sonorous rales. Some decrease of breath sounds with faint crackling rales at left base laterally. Diagnosis: Metastasis to lungs; probably less fluid than before.

On December 31, 1923, roentgen-ray plate of chest: "Previous report confirmed; sarcoma metastasis. Deposits throughout right side" (Fig. 1).

The patient died, February 9, 1924, at home, a little over two months following the onset of the lung symptoms.

CASE II.—G. H. W. a white man, aged forty-seven years, who had developed a small sore on the lower lip about two years before and who had been treated elsewhere for one year by various measures, including high frequency electric current, violet-ray, cautery,

roentgen-ray and excision of the lip tumor, under a clinical diagnosis of "skin cancer." Treatment had been continued at Memorial Hospital with radium, also under a clinical diagnosis of carcinoma of the lip. However, tissue removed from the left submaxillary region on April 23, 1923, in the course of a submaxillary dissection was reported as showing a "large spindle-cell fibrosarcoma of neurogenic type."

When the patient was seen on March 28, 1924, he had been readmitted with a note that he had recovered from an attack of pneumonia at his home about six weeks before, and that his general condition was as a result somewhat below normal. There was still a non-ulcerated plaque of tumor tissue in the musculature of the chin $3\frac{1}{2}$ by 2 by $\frac{1}{2}$ cm.

Examination of the patient on March 28, 1924, revealed dulness with diminished breathing and a few crackling rales, together with some change in voice sounds at the right base. Similar changes, but less marked, were also present in the left interscapular region. There was a soft subcutaneous nodule on the left chest wall, a soft lump over the spine of the right scapula and another lump, possibly a lipoma, over the lumbar region. (The first two lumps resembled neurofibromas in their consistence.)

As the case was still being treated under a clinical diagnosis of of carcinoma of the lip, the marked discrepancy between this and the pathological report raised the question whether slides might not have been mixed in the laboratory. However, the signs described above were consistent with pulmonary metastasis, and if the patient really had neurogenic sarcoma of the lip (a rare tumor) there was more reason to fear lung metastasis than there would be if he had carcinoma of the lip. Therefore the following comment was made: "Signs may indicate a residuum of a pneumonia, but if the pathological report of neurosarcoma refers to this case, question of lung metastasis should be investigated further, and I would suggest getting a roentgen-ray plate." It was felt, too, that the presence of the subcutaneous nodules having a consistence like that of neurofibromas tended to confirm a diagnosis of neurogenic sarcoma, because a certain proportion of cases of neurofibromatosis develop sarcoma.

On March 31, 1924, a roentgen-ray plate of the chest revealed "evidence of sarcoma metastases."

The patient was discharged on April 2, and died, May 3, 1924, a little over two and a half months after the onset of his supposed pneumonia.

CASE III.—Mrs. C. R., a white woman, aged thirty-five years, had been treated at Memorial Hospital since January 2, 1924, for carcinoma of the cervix. (Pathological report: Plexiform epithelioma.)

Right

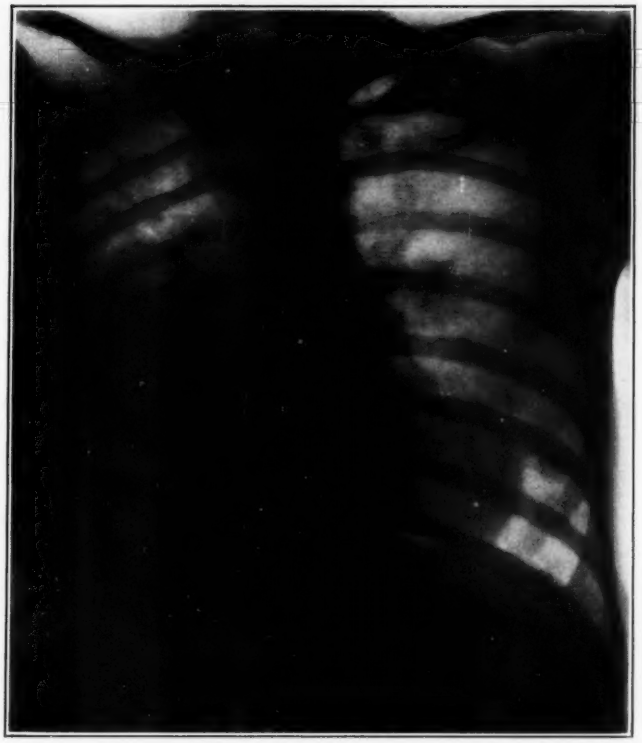
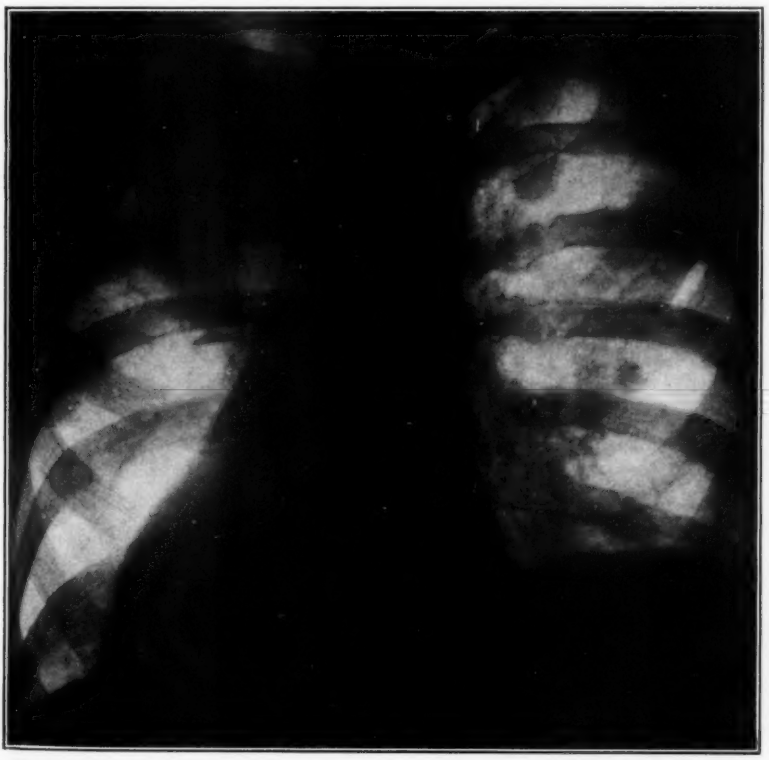


FIG. 1.—Case I. Roentgen-ray plate made, December 31, 1923, confirming the finding of evidence of sarcoma metastases in the previous plate of December 7, 1923.



Right

FIG. 2.—Case II. Plate taken, March 31, 1924, revealed evidence of sarcoma metastases.

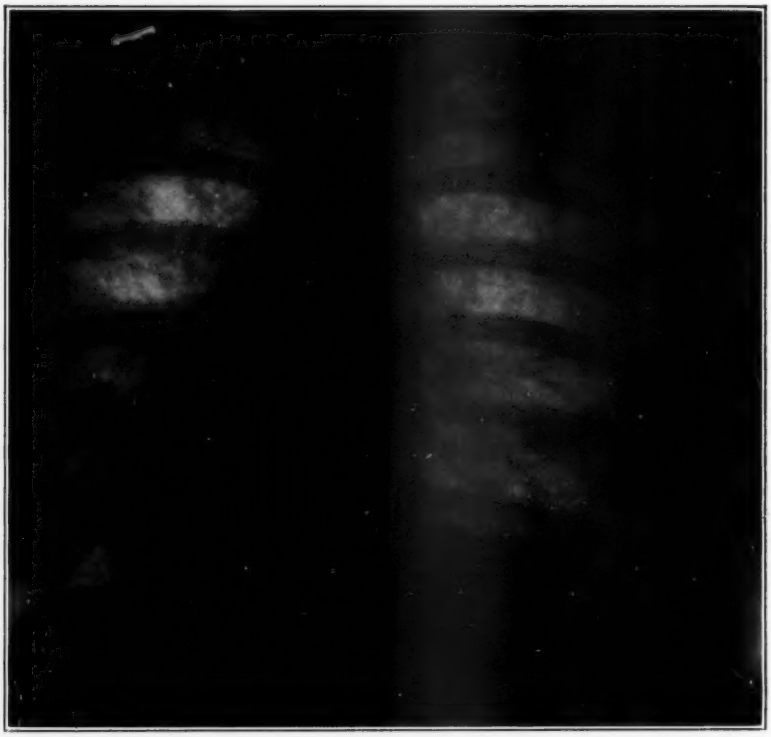


FIG. 3.—Case III. Plate made, June 19, 1924, showing numerous discrete circular dense shadows in the bases, also peribronchial infiltration throughout the lungs, most marked on the right. Patient died in less than three months afterward, suffering from pulmonary and pleural symptoms.

The writer was asked to see her on June 20, 1924, on account of a severe cough and pain in her chest. The history with respect to her lung condition was as follows: Her mother had died twenty-four years before of tuberculosis. No other member of the patient's immediate family had ever had tuberculosis, to the best of her knowledge. She had had no miscarriages. Five years before, during the influenza epidemic, she had had pneumonia, with complete recovery, and no subsequent cough. Her present pulmonary complaint began about March, 1924 (three months previously), and first appeared in the form of a persistent cough. There was expectoration of "phlegm," but no hemoptysis. Four weeks before there was a *sudden onset* of "pleurisy" without any history of exposure; the symptoms had been pain in the *right* chest, with a temperature of 102° F. The fever lasted two days. She was in bed one week. When the writer examined her, on June 20, she complained of continual severe cough and of having had a severe pain in her *left* chest posteriorly for the past three days.

The examination of her chest showed marked diminution of breath sounds at the bases all around, and in fact over the lower one-half or two-thirds of each lung posteriorly, without definite changes in the percussion note, tactile fremitus or voice sounds. Occasionally a faint crackling rale was heard at either base. Sibilant rales were heard high up in the left axilla. Slight changes in breath sounds were heard over the left upper lobe anteriorly. Her general appearance was good. From the history and physical signs a diagnosis of metastasis to the lungs was ventured.

A roentgen-ray plate of the chest made at the same time was reported as follows: "Chest plate reveals the presence of multiple rather discrete circular dense shadows in the bases, with evidence of peribronchial infiltration throughout the lungs, most marked in the right, with considerable thickening of pleura. Probably metastases, although bronchopneumonia or miliary tuberculosis should be excluded clinically" (Fig. 3).

The writer felt that bronchopneumonia and miliary tuberculosis could be excluded clinically, considering all the features of the history and the physical examination. It might be noted here that neither during this admission nor during her stay at the hospital in January had she shown any fever, and her pulse and respiratory rate were normal.

She was discharged, June 21, 1924. The next note on her chart is that she was reported on September 5, 1924, as being very ill and confined to bed at home under the care of her family physician for "pleurisy." Sometime between then and September 22 it was reported that she had died.

Discussion and Conclusions. With closer observation of the course of cases of pulmonary metastasis and more careful analysis of their history, we are beginning to feel that a considerable proportion of

these cases have a more or less acute onset, varying all the way from simulation of mild bronchitis or pleurisy to the most severe forms of acute respiratory disease. Unfortunately, the actual onset of the respiratory symptoms is not often observed by those who are concerned with the primary tumor. In many cases no physician is consulted at the onset, especially if it is comparatively mild. In other cases in which the onset is more stormy the family physician or some general practitioner who is not fully cognizant of the existence or the potentialities of the primary tumor may be called, and under the stress of the urgent need for treatment both physician and patient may overlook the importance of the history of a malignant tumor. Moreover, in view of our experience, it seems justifiable to say that, although the simulation of acute respiratory diseases by secondary lung tumors has been described by several writers, its description has found its way into comparatively few text-books, and it does not seem that the profession at large is sufficiently on its guard against this infrequent yet important source of diagnostic and prognostic error. The diagnosis is, of course, much more difficult when the primary tumor is concealed, but if the possibility were always kept in mind that any case with acute respiratory symptoms may be suffering from pulmonary metastases of some malignant tumor (or, for that matter, a primary lung tumor), the chances of error would be much less.

REFERENCES.

1. Craver, L. F.: The Value of Physical Signs in the Early Detection of Pulmonary Metastases, Am. Jour. Med. Sci., 1924, **167**, 852.

2. Roberts, F. T., and Perkins, J. J.: New Growths of the Lung, Allbutt and Rolleston's System of Medicine, London, 1912, **5**, 502.

3. Manges, M.: The Roentgen-ray in the Diagnosis of Pneumonia, Pleural Diseases and Pulmonary Tumors, New York Med. Jour., 1917, **106**, 917.

4. Stokes, W.: A Treatise on the Diagnosis and Treatment of Diseases of the Chest, New Sydenham Society, London, 1882, p. 385.

5. Holt, O. P., and Rattermann, H. T.: Multiple Metastatic Sarcomas of Lungs, Jour. Am. Med. Assn., 1916, **66**, 171.

6. Robey, W. H.: Malignant Disease of the Lungs, Med. Clin. North America, 1921, **4**, 1811.

7. Burt, S. S.: Multiple Metastatic Sarcomata of the Lungs, Philadelphia Med. Jour., 1900, **6**, 545.

8. Oliver, P.: Metastatic Sarcoma of Lung with Hypertrophic Pulmonary Osteoarthropathy, Surg. Clin., 1918, **2**, 361.

9. Beger, A.: Ein Fall von secundärer acuter Miliarcarcinose der Lungen, Deutsch. Arch. f. klin. Med., 1879, p. 357.

10. Bard, L.: Carcinosis of the Lungs, Rev. méd. de la Suisse romande, 1918, **38**, 1; Abstract, Jour. Am. Med. Assn., 1918, **70**, 964.

11. Sternberg, M.: Lungengeschwülste, Wien. med. Wchnschr., 1923, **73**, 1366.

12. Rolleston, H. D., and Trevor, R. S.: A Case of Primary Sarcoma of Lung, Simulating Empyema, Brit. Med. Jour., 1903, **1**, 361.

13. Marfan, A. B.: Cancer du poumon et de la plèvre, Tr. de méd. (Charcot, Bouchard and Brissaud), Paris, 1893, **4**, 534.

14. Bard, L.: La lymphangite pulmonaire cancéreuse généralisée, Semaine méd., 1906, **26**, 145.

15. Osler, Sir W.: The Principles and Practice of Medicine, 8th ed., 1917, p. 653.

16. Tyson, J., and Fussell, M. H.: The Practice of Medicine, 6th ed., Philadelphia, P. Blakiston's Son & Co., 1914, p. 534.

17. Hellendall, H.: Ein Beitrag zur Diagnostik der Lungengeschwülste, Ztschr. f. klin. Med., 1899, **37**, 435.
18. Fowler, J. K., and Godlee, R. J.: The Diseases of the Lungs, London, 1898, p. 488.
19. Martin, T. M.: Metastatic Sarcoma of Lung Simulating Pneumonia, Brit. Med. Jour., 1913, **2**, 939.
20. Mix, C. L.: Carcinoma of the Lung, Med. Clin. North America, 1922, **5**, 1681.
21. Laennec, R. T. H.: Traité de l'auscultation médiate, 1826, **2**, 368 (cited by).
22. Unverricht: Beiträge zur klinischen Geschichte der krebsigen Pleuraergüsse, Ztschr. f. klin. Med., 1882, **4**, 79.
23. Dieulafoy, C.: A Text-book of Medicine, translated by V. E. Collins and J. A. Liebman, London, 1912, **1**, 289.
24. Montel and Hauvuy: Secondary Cancer of Lung, Néoplasmes, Paris, 1923, **2**, 155; Abstract, Jour. Am. Med. Assn., 1923, **81**, 1396.
25. Zinn, W.: Lungenmetastasen bei Chorionepitheliom einer 31 jährigen Frau, mehrere Wochen (etwa 7) hindurch unter einem der Miliartuberkulose ähnlichen Krankheitsbilde verlaufend, Deutsch. med. Wchnschr., 1908, **34**, 713.
26. Pässler: Ueber das primäre Carcinom der Lunge, Virchow's Arch. f. Path. Anat., 1896, **145**, 239.

CILIARY INHIBITION OR DESTRUCTION IN TRACHEOBRONCHIAL ASTHMA, WITH NOTES ON BRONCHOSCOPIC TREATMENT.

By William F. Moore, M.D.,

BRONCHOSCOPIST, DEPARTMENT OF DISEASES OF CHEST, JEFFERSON HOSPITAL, PHILADELPHIA.

The object of this paper is to present results of bronchoscopic, histologic and bacteriologic studies in a series of cases from the Bronchoscopic Clinic of the Jefferson Medical College Hospital of Philadelphia. The majority of these cases are of many years' duration and marked severity. Many have been studied thoroughly in the other special clinics of the hospital.

Theories as to the causative factors which are thought to produce attacks of tracheobronchial asthma are legion, and time and space do not permit of their enumeration. One is impressed on reviewing the clinical material, and on bronchoscopic examination, with the fact that more than one cause underlies this condition.

The speedy relief afforded the great majority of our cases has led us to believe that bronchoscopy alone, affording as it does a means of cleansing the overloaded mucous membrane of the tracheobronchial tree, temporarily alleviates the symptoms and yields relatively permanent results in many cases. This would seem to justify the conclusion that defective ciliary drainage is a factor of the utmost importance.[1, 2]

The question as to whether infection of the bronchi is primary or secondary is one of great importance, but difficult of solution. Our help in this must come from the internist and specialist who can point out the possible source. Primary cases have responded

permanently to this form of treatment; secondary cases require, of course, eradication of, or treatment at, the source.

Technic. Asthmatic patients referred for diagnostic bronchoscopy and treatment are first given a complete physical examination by the internist. Roentgen-ray studies are then made. As the majority of these cases have come through the asthma clinic, sensitization tests have been completed. No patient is bronchoscoped without having had a physical examination and roentgen-ray studies.

At the first examination morphin is generally administered hypodermically in doses of from $\frac{1}{8}$ to $\frac{1}{4}$ gr. one hour before bronchoscopy. No general anesthetic has ever been found necessary. In children no cocain is used, but in adults a 10 per cent solution is applied deep enough in the pharynx to inhibit the function of the superior laryngeal nerve.[3] This is applied by means of a swab on a curved applicator forceps and repeated once.

There is no contraindication to a bronchoscopic examination during an asthmatic attack in the type of cases herein referred to. Preliminary medical examination has usually eliminated so-called "cardiac asthma" and other conditions in which there is no indication for bronchoscopy.

Collection tube for aspirated material.

Bacteriologic Specimens. Specimens are obtained bronchoscopically, uncontaminated by oral secretion, by two means: Either by swab or, where the secretion is not too viscid and is susceptible of aspiration, it is drawn into specially devised tubes which are inserted between the aspirating bronchoscope and the rubber tube from the suction pump. The tubes are sealed for laboratory examination later. Specimens are immediately "planted" on human blood agar-agar and slide smears made by Dr. George R. Moffitt, one of the group, who will present the results of his work in another paper.[4] An abstract of some phases of his work is given in a subsequent paragraph.

Bronchoscopic Treatment. Two methods are employed to rid the mucous membranes of the trachea or bronchi of their overload of secretion, namely, sponging where the secretion is thick and tenacious or by aspiration, either through the special aspirating bronchoscope or with a separate aspirating tube inserted through and beyond the bronchoscope. Forceps are ordinarily not required for

this. A solution containing 10 drops of a 10 per cent solution of cocain and 20 drops of adrenalin solution (1 to 1000) in 1 fluid-ounce of normal saline as a vehicle is then instilled, using 5 cc in each main stem bronchus. A 10 per cent solution of silver nitrate has been applied to localized areas in certain cases and in others guaiacol in 5 per cent and gomenol in 20 per cent strength have been used. However, the adrenalin-cocain combination above mentioned, which we know as the "asthma solution," is the one most frequently employed.

Admission to hospital is not required, and the number and frequency of treatments generally depends, after the first two bronchoscopies, on the character and frequency of the asthmatic attacks, the patient being instructed to report at weekly intervals, so that accurate data may be kept. Some patients require but three or four bronchoscopic treatments, while others have needed as many as eighteen.

Vaccines. One week after the diagnostic bronchoscopy (at which specimens are taken) the autogenous vaccine is ready for administration. This is given at four-day intervals in ascending dosage, as outlined by Dr. Moffitt. This part of the treatment is either carried out by the physician referring the case, or the patient returns to the asthma clinic for its administration.

Bacteriology and Vaccines. Among the various organisms the Streptococcus viridans, Streptococcus hemolyticus or a hemolytic strain of the Staphylococcus aureus, in pure culture or associated, are conspicuously present in nearly all cases of asthma. Their role may be (*a*) causative factors, or (*b*) secondary invaders responsible for a primary bronchitis upon which the asthma develops. It is reasonable to believe, and this belief is supported by our results, that the use of autogenous vaccines prepared from the organisms found would give promise of establishing, as permanent, the relative cures which have been effected by local treatment, especially by the assistance of ciliary drainage to be accomplished by bronchoscopic aspirations.

The organisms recovered from the secretions of asthmatics, removed by the bronchoscope without oral contamination, show a marked degree of attenuation, which may account for the non-occurrence of metastatic infection. This does not, however, render vaccines prepared from them less potent, for loss of virulence of an organism does not, in any way, affect the efficiency of the vaccine.

Classification of Cases. From the standpoint of results obtained it has seemed logical to assume that the twenty-seven cases herein reported should be grouped in a broad, but convenient, classification, as: (1) Those with bronchoscopically evident active suppurative tracheobronchitis;[1] (2) those with a bronchoscopically evident chronic passive congestion. In the first group are placed

all those showing an inflammatory mucosa with a great deal of secretion. In the latter are placed those cases in which the mucosa has assumed the bluish-red, leathery appearance, with little or no secretion, or those with inspiratory or expiratory collapse of the bronchi, also with little secretion. It has seemed to us that a true infection was responsible for the major (first) division, while in the second group factors outside the tracheobronchial tree were responsible for a continuation of the symptoms; and the local infection, if any, was secondary and played a minor role in causing attacks. We are cognizant of the fact that this division is open to criticism from many angles, and that the borderline is rather hazy in some cases; still it is necessary for workers in this field to have some criteria for classification that may serve as a basis for therapeutic indications from which they may reasonably expect to get results.

TABLE I.

CLASS I.—TRACHEOBRONCHITIS PRESENT.

No.	Result.
3	Great improvement; no attacks in eight months.
4	Improved.
5	Improved
6	Improved.
9	Marked improvement.
10	Improved; no attacks in four months.
11	Improved.
12	Greatly improved
13	Greatly improved.
14	Improved.
15	Improved.
16	Improved; no attacks in two years.
17	No change.
19	Pansinusitis; referred for diagnostic bronchoscopy only.
20	For diagnostic bronchoscopy only.
21	Attacks decreased in severity and frequency.
22	Improved; one attack in four weeks.
23	Improved; no symptoms for one month before discharge.
26	Improved.
27	For diagnostic bronchoscopy only.

CLASS II.—TRACHEOBRONCHITIS ABSENT.

1	Temporary relief.
2	Temporary relief.
7	No relief; probably due to a postpneumonic suppuration.
8	Unimproved; diagnosis; cardiorenal disease.
18	No change.
24	Temporary relief only.
25	Referred for treatment for pansinusitis.

Reports of Cases. In presenting the following tabulations of cases it will be noted that none has been pronounced cured, although two years have elapsed in one case since having an attack. When a case can be pronounced permanently cured seems justly to be a much mooted question with the internists. It would seem that for

the purposes of determination of the efficiency of treatment a patient free from attacks for a year might be called a relative cure.

Ciliary Movements and Histology of Ciliated Cells. Dr. George R. Moffitt[4] has made a most interesting and important report of the results of his work with us at the Bronchoscopic Clinic in a paper on the pathologic histology and bacteriology of asthma. With his permission we here present some of his observations which are pertinent to our subject:

"The bronchial columnar epithelial cells are 40 to 50 micra long and 10 to 14 micra in diameter. Together with these cells are ciliated spherical cells which do not appear to be the goblet cells that are normally present in the bronchial mucosa.

"There are as many as 480 cilia attached to a cell. Works on histology have given the number as 12 to 25. The ciliary movements are at the rate of 360 a minute or 6 a second. There is a secondary ciliary movement which forces secretion and foreign particles from the bronchial wall into the lumen. The cilia are 18 to 20 micra long. The only reference found upon this subject gives 3 to 5 micra as their length.

"The basal or root process (not mentioned by any treatise on histology) apparently connects the cells of the free edge or uppermost layer to the basement membrane.

"One or more of the following changes occur in the ciliated columnar epithelial cells of the asthmatic: (1) Loss of the ciliary motion which produces a current; (2) complete loss of ciliary motion; (3) actual loss of the cilia; (4) fatty degeneration of the cell.

"*Regeneration of Ciliated Epithelium.* The question arises as to the character of regeneration of the destroyed epithelial cells and repair of the injured bronchial mucous membrane. It is a well-known pathologic fact that mucous membrane, in general, regenerates more rapidly and more perfectly than any other tissue. At the same time it is uncertain as to whether a cell from which the cilia have been removed by trauma or disease could replace those lost processes by new ones.

"There seems to be no reason why this should be considered impossible, and our observations lead us to believe that replacement of cilia or ciliated cells, lost by disease, with new cilia or new ciliated cells does take place. The cilia, as has been stated, are connected with delicate intracellular fibrillæ within the superficial parts of the cell and are in all probability continuous with these fibrillæ, each of which in turn is connected with and controlled by two-minute bodies of centrosomic derivation. It is not inconceivable that when a cilium is lost these bodies may cause the fibrillum to grow and extend beyond the cuticula as a new cilium. This would be a repetition of the process that goes on in each normal nonciliated cell as it reaches the free surface of the stratified layer of cells, for the cells beneath the surface, as has been previously stated, possess no cilia.

TABLE II.

No.	Duration in years.	Solution used.	Appearance.	Secretion.	Bacteria.	Roentgen-ray examination.	No. of broncho-scopies.	Result.
1	20	Cocain-adrenalin	Inflamed and velvety; secretion present	Small amount	Str. viridans	Peribronchial thickening; root shadows dense	2	Improved; the symptoms not returned.
2	4	Cocain-adrenalin; 20 per cent gomenol	Local inflammation; collapse of post wall	Very little	.....	Thickening at roots and right lower lobe	4	Improved; no return to date.
3	1	Gomenol (20 per cent)	Trachea and right bronchi inflamed; right bronchi dilated	Visible; bronchi and right lung	Str. viridans, B. influenza; Str. hemolyticus	Thickening of roots and left lower lobe	15	Discharged; no symptoms for ten months.
4	9	Cocain-adrenalin	Chronic inflammation of bronchi mucosa; secretion present	Tenacious and scant	Str. viridans; Sta. aureus	Peribronchial thickening of right lower lobe	4	Improved; no return in ten months.
5	9	Cocain-adrenalin	Bluish-red	Small amount	No culture	Dense right upper and middle lobes	5	Improved temporarily only.
6	5	Cocain-adrenalin	Mucosa inflamed	Dry	.....	Root shadows heavy	7	Improved; died of intercurrent disease.
7	15	Argyrol (20 per cent)	Congested and edematous	Thick and adherent	.....	Fibrosis of lower right lung	2	Unimproved.
8	1	.....	Bluish-red	None	No culture	Fibroses of both bases	4	Improved, temporarily only.
9	2½	Gomenol and cocain-adrenalin	Inflamed and grayish-white	Tenacious	Str. viridans; Sta. aureus	Thickening at roots	18	Improved; no attacks for four months.
10	15	Cocain-adrenalin	Injected and bluish-red	Quite viscid	Str. hemolyticus	Few dense lymph glands; no thickening	12	Improved.
11	3	Cocain-adrenalin	Inflamed trachea and bronchi	Present throughout	.....	Slight thickening at roots	..	Improved.
12	2	Cocain-adrenalin and 10 per cent nitrate locally	Bronchial orifices normal	Very thick	Str. viridans; Str. hemolyticus	Thickening at roots	..	Greatly improved.
13	2	Cocain-adrenalin and K. I.	Normal	Thick and viscid, only in middle lobe bronchus of right side	No culture	Peribronchial thickening at right lower lobe	16	Improved.

14	2	Cocain-adrenalin	Mucosa injected	Tenacious	Str. viridans	Peribronchial thickening	3	Improved.
15	3	Cocain-adrenalin	Red and injected	Large anount and sticky	Str. viridans; Str. hemolyticus	Thickening at roots	2	Improved.
16	12	Cocain-adrenalin	Red and injected; collapse of posterior wall	Thick and tenacious	.....	Peribronchial thickening	2	No attack in two years.
17	17	Cocain-adrenalin	Trachea and right main stem bronchus inflamed	Thick and tenacious mucopus	No culture	Peribronchial thickening, general, at roots	2	No change.
18	10	.....	Red and inflamed	Gelatinoid	.....	.....	1	No change.
19	..	Cocain-adrenalin	Inflamed and velvety	Plastic	No culture	Thickening at roots; peribronchial thickening		
20	39	Cocain-adrenalin	Small amount of thin secretion over the trachea and bronchi	Elastic	Str. viridans	Peribronchial thickening of both upper lobes	..	For diagnosis only.
21	18	Cocain-adrenalin	Patchy area of inflammation	Small amount and tenacious	Sta. aureus (hemolytic)	Peribronchial thickening of right upper and lower lobe	9	Improved; attacks decreased in their frequency.
22	10	Cocain-adrenalin	....	Thick and tenacious	Str. viridans; Sta. hemolyticus	Peribronchial fibrosis of upper lobes	7	Improved; one attack week the treatment was omitted.
23	4	Cocain-adrenalin and 2 per cent guaicol and 20 per cent gomenol	Mucosa cyanotic and edematous; collapse on expiration	Pus was exuding from all bronchi	Str. viridans; Sta. hemolyticus; M. cinereus	Peribronchial thickening and fibrosis of entire chest	17	Discharged to work, and no symptoms since May 7, 1924.
24	5	Cocain-adrenalin	Bluish-red in carinal region	Mucus high in trachea	.....	Thickening at roots	2	Improved
25	Many	Cocain-adrenalin and silver nitrate	Mucosa inflamed and edematous	Thin, mucoid	.....	.....	6	Unsatisfactory; improved.
26	Many	Cocain-adrenalin and 10 per cent silver nitrate, locally	Inflamed	Thick and tenacious	Sta. aureus (hem.) and M. cinereus	Thickening at roots	13	Improved.
27	..	.....	Inflamed and edematous; no marked collapse on expiration	.....	.....	Root structures heavy and fibrosis of left lower, right, middle and lower lobe	1	For diagnosis only.

"However, if it is true that lost cilia cannot be replaced by new ones, the general process of repair of the bronchial mucosa would not be long delayed, for the injured surface cells would soon be exfoliated, as are all surface cells of stratified epithelium, squamous or columnar, and their places taken by the underlying cells which would acquire their cilia by the ordinary physiologic process, whatever that may be.

"If the destructive process were deeper than the epithelium, involving the basement membrane and tunica propria, an ulcer would result and the process of repair would involve the formation of granulation tissue, new fibrous tissue and the proliferation of new epithelial cells from the uninjured cells at the edge of such ulcer.

"Deep ulceration, however, as has been repeatedly demonstrated by bronchoscopy and autopsy, does not occur in asthma."

Summary. 1. Practically all cases which have come to us for treatment have shown on roentgenographic study peribronchial thickening to a marked degree in some part of the lung; in some cases general.

2. Those cases associated with a demonstrable tracheobronchitis have responded best to bronchoscopic treatment.

3. Ridding the tracheobronchial mucous membrane of secretion will in itself temporarily benefit all cases.

4. While temporary relief follows these bronchoscopic treatments, permanent relief necessitates intrabronchial medication; the administration of vaccines made from the organism recovered directly from the bronchial secretions; a general attention to hygiene and an abundant diet, the same as for tuberculous patients.

5. Regeneration of the ciliated epithelium occurs very rapidly after the secretion, which as inhibited its action, has been removed either by aspiration or swabbing.

6. Impairment of ciliary action has been conclusively demonstrated. Its restoration is imperative for lasting improvement.

BIBLIOGRAPHY.

1. Jackson, Chevalier: Suppurative Diseases of the Lung; Bronchscopic Drainage as an Aid to Treatment by the Internist, Trans. Am. Acad. Ophthal. and Oto-Laryngol., 1923, **28**, 337.

2. Jackson, Tucker, Clerk, Lukens and Moore: Bronchoscopy as an Aid to the Thoracic Surgeon, Jour. Am. Med. Assn., 1924, **84**, 97.

3. Moore, W. F.: Pulmonary Abscess, Jour. Am. Med. Assn., 1922, **78**, 1279.

4. Moffitt, G. R.: Pathological Histology and Bacteriology in Tracheobronchial Asthma (in press).

CHRONIC MEDIASTINITIS.

By Leila Charlton Knox, M.D.,
ASSISTANT ATTENDING PHYSICIAN, ST. LUKE'S HOSPITAL, NEW YORK.

Mediastinitis is a condition which, though always mentioned in academic discussions of thoracic disease, rarely assumes any great interest either clinically or pathologically, so much more often are symptoms referable to organs rather than to their supporting tissues. As a cause of death the disease is certainly infrequent, if we include only those cases in which the condition is not associated with a serious lesion of heart, vessels, bronchi or nodes.

Everyone is familiar with the effects of primary or metastatic neoplasms which give rise to thoracic symptoms, but the present paper deals only with a smaller group of cases, unquestionably inflammatory, in which the mediastinal lesion far exceeds both in extent and activity any other manifestation of disease. These cases may usually be differentiated pathologically and clinically from so-called indurative and mediastino-pericarditis, for the latter, while occasionally resulting in great fibrous thickening of the mediastinal tissues, also involves especially the pericardium from which it proceeds.

The condition is probably nearly always due either to tuberculosis or syphilis; but very rarely other agents which produce granulomata, such as the mycoses, may be the excitants, or an interstitial form of Hodgkin's disease may give rise to mediastinal symptoms. These two are unusual. Scarlet fever, measles, and acute rheumatic fever have each been said to have given rise to productive mediastinal lesions, and in these cases it is possible that a streptococcus is the invading organism.

The symptoms are due to compression or invasion of important structures, and therefore may be either anatomical or reflex physiological phenomena. In such a case observations of the underlying lesions may contribute directly to our understanding of clinical symptoms.

Clinical History. The patient was a negro woman, aged twenty-seven years. She was admitted to St. Luke's Hospital on the medical service then in charge of Dr. F. Warner Bishop, to whom I am indebted for the clinical notes.

Upon arrival the patient was thought to be in fair general condition, and a tentative diagnosis of bronchial asthma was made, but the onset of extreme dyspnea shortly showed her to be by no means out of danger, and she died of respiratory failure, less than twenty-four hours after her entrance into the institution. For this reason only a brief history is available, and few pathological examinations had been made. Unfortunately blood for a Wassermann reaction had not been taken.

The history stated that her chief complaint was recurrent attacks of nausea and vomiting, occurring over a period of ten months. The first attack had begun after eating, and was followed by retrosternal pain and wheezing inspiration, with slight hemoptysis. There was no fever, but the patient had been so prostrated as to be unable to work for one week. A similar attack had occurred two months later, and since that time there had been increasing nausea and distaste for certain foods. For one week before her admission there had been frequent vomiting, induced at times even by taking water.

In spite of the predominance of gastric symptoms in this history, her chief difficulty when seen by the ambulance physician was extreme dyspnea, and although expiration was labored, inspiration was still more difficult.

The physical examination showed a young colored woman with eccentric, irregular pupils, which reacted sluggishly to light and accommodation. The lungs were resonant and the breath sounds wheezing and asthmatic, with dry sonorous rales throughout, more on the right side. Other physical signs were normal.

The blood count was normal. The urine contained considerable acetone. The systolic blood pressure was 130 mm., but the usual cycle of changes in the sounds could not be detected and no diastolic level could be determined. A provisional diagnosis of bronchial asthma, due to foreign protein sensitization, was considered, although the unequal pupils suggested a syphilitic infection, and the possibility of an aneurysm was kept in mind. The roentgenogram of the thorax, showing the trachea displaced to the left, seemed to confirm this idea (Fig. 1). Death followed the morning after admission, and an autopsy was performed two hours later.

Gross Pathology. At autopsy the positive findings were as follows: inequality of the pupils and pigmented, parchment-like scars on the dorsa of the feet, the legs and the chest. The liver was attached to the diaphragm and the anterior abdominal wall by numerous rather fresh, veil-like, fibrous adhesions. The capsule was slightly thickened and section showed slight changes due to chronic passive congestion. The gall bladder was small, the wall somewhat thickened, and the bile within it inspissated and tenacious. The spleen likewise showed numerous fibrous adhesions to the surface, a thickened capsule, much fibrosis, and very much diminished lymphoid markings. Both kidneys were smaller than normal, the left weighing 75 gm. and the right 100 gm. The capsules were somewhat adherent and there were depressed scars scattered over the surfaces of both. The left ovary contained a small dermoid cyst.

Both lungs were attached at the apices by fibrous adhesions. The right did not reach to the diaphragm, a small quantity of air undoubtedly being present in this pleural cavity, as was indicated

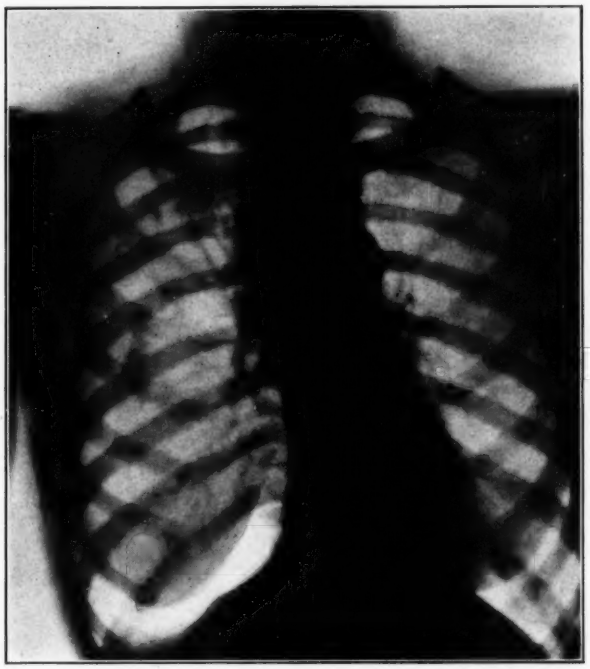


FIG. 1.—Roentgenogram of thorax, showing moderate widening of the mediastinal shadow and the prominent convexity of the aorta which was rotated anteriorly and the trachea displaced to the left. Pneumothorax, right pleural cavity.

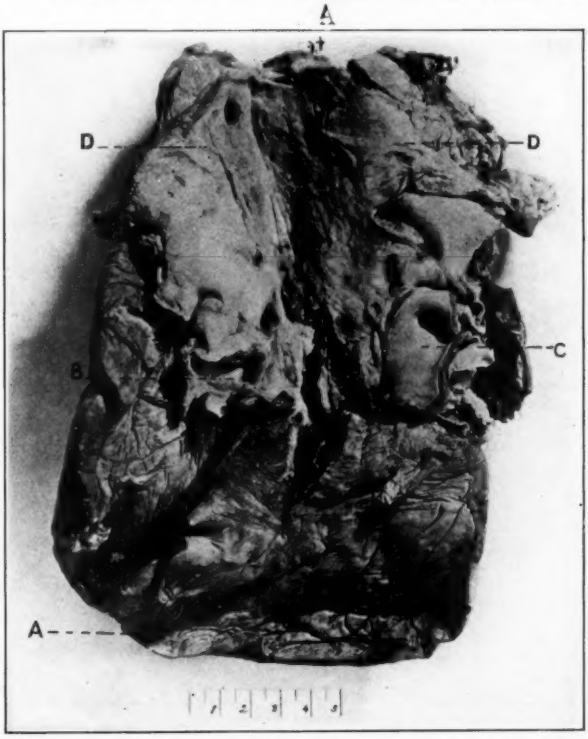


FIG. 2.—Photograph of right lung, aorta and the fibrous mass in the mediastinum surrounding all structures. *a*, Right lung; *b*, right auricle; *c*, ascending aorta; *d*, tumor-like mass in mediastinum.

FIG. 3.—Photomicrograph of typical area of the mass, showing the broad keloidal strands of hyaline tissue.

FIG. 4.—Granulomatous area with masses of round cells and necrotic zone with fragmented and pycnotic nuclei.

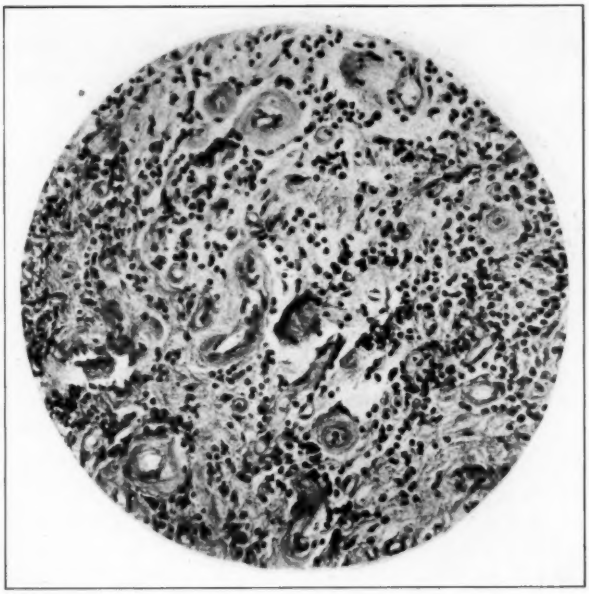


FIG. 5.—Photomicrograph of a vascular field, all the vessels having extremely thick hyaline walls.

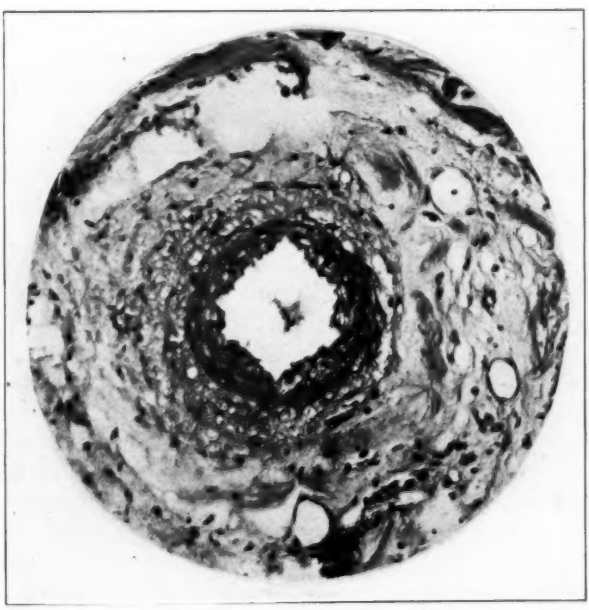


FIG. 6.—High-power photomicrograph of an artery, showing marked endarteritis and degeneration of the media and adventitia.

by the roentgenogram. Both lower lobes were dry, well aërated, and in small areas emphysematous, rupture of an air vesicle probably accounting for the pneumothorax. The bronchioles contained no mucus or other exudate. The right upper lobe was small, firm, poorly expanded, and densely adherent to the large mediastinal mass which formed the most conspicuous feature of the thoracic contents (Fig. 2). There was a small amount of bronchopneumonia in this region, extending outward from the medial surface of the lung for a distance of 1 to 2 cm. with an especially dense fibrous mass beneath the apical adhesions, an area suggesting organizing pneumonia. This entire upper lobe was somewhat atelectatic, while the middle and lower ones showed compensatory emphysema. The entire superior and middle, and part of the dorsal mediastina were completely filled with a solid tumor-like mass, about 6 cm. in thickness anteroposteriorly. It extended from the suprasternal notch to the pericardium and protruded anteriorly nearly to the sternum, presenting a hard, rounded convexity, at first suggesting an aneurysm, though very much more resistant. All the structures of the middle mediastinum were adherent or included within the mass, the aortic arch was displaced to the left of the median line and twisted into the anteroposterior plane. The aortic wall, however, was only loosely adherent to the mass, except at the root of of the neck, where the left common carotid was also invaded and constricted. The right innominate artery was thus forced to take an oblique course across the root of the neck, and both it and the right carotid could scarcely be separated from the inflammatory tissue. The trachea was displaced to the left, as had been noted in the roentgenogram of the thorax. The left innominate artery was relatively unaffected. The left bronchus was infiltrated, especially over the inferior and anterior portions of its circumference. The right main bronchus, however, was much more seriously infiltrated and constricted, and was held rigidly fixed in the new tissue, while its lumen, not half a centimeter in diameter, could only be opened with difficulty with the point of the scissors.

The superior vena cava was surrounded and infiltrated throughout the whole of its course, more completely, however, posteriorly than elsewhere, as a solid mass of the growth intervened between it and the pericardium. The lumen of the artery was not completely obliterated, but admitted only a small probe, and the great induration and inelasticity of the mass seemed to prevent any expansion of the venous wall. The endothelium, however, remained smooth. The right internal jugular vein was constricted at its inferior end just above the point of its union with the subclavian. The left innominate vein was greatly encroached upon by the mass throughout the lower 2½ cm. of its course, its lumen reduced to a mere slit, and, like the superior vena cava, nonexpansible, though not thrombosed.

The right vagus nerve was displaced forward and at the level of the subclavian artery entered the fibrous tumor, from which it could not be dissected. The recurrent laryngeal nerve on the right side was also so infiltrated that it could not be traced below this level, the fibrous tissue reaching to the trachea. On the left side the recurrent laryngeal remained free, and the left vagus nerve was relatively uninvolved. Fatty tissue representing the atrophied thymus gland and small lymph nodes in the ventral mediastinum were not involved, but numerous anthracotic bronchial nodes were completely surrounded by, and firmly embedded in, the inflammatory tissue.

Microscopical Pathology. Sections of the mass show an enormous mediastinal overgrowth of connective tissue far beyond any which we commonly see in fascial planes, and certainly beyond any reparative demands. The tissue is almost entirely fibrous, presents few nuclei, and has very limited blood supply (Fig. 3). Some of the foci of lymphocytes and other cells undoubtedly represent fragments of lymph nodes, but other areas are granulomatous (Fig. 4). The sections show uniformly a preponderance of broad hyaline connective tissue strands such as are seen in keloids, indeed one wonders whether the process is not to be regarded as of much the same type. It seems probable that infection caused an initial inflammatory reaction which, in healing, provided an extraordinary amount of connective tissue, and that hyalin degeneration supervened to the same extent as appears quite regularly in cutaneous scars in the negro race.

Nerves are compressed and infiltrated to the point of atrophy, and the vessel walls are constricted and their lumina much reduced. Groups of small newly formed vessels with intact endothelium and homogeneous, collagenous, outer walls are seen (Fig. 5). The walls of the older arteries are thickened by proliferation of the subendothelial fibrous tissue, and degeneration of the media has extended so far that it is difficult to recognize each coat (Fig. 6). The thoracic aorta shows an extraordinarily diffuse degeneration of the media, chiefly myxomatous. The other coats are little affected. Extensive perivascular infiltration is seen only in the adventitia of the aorta.

The apical lesion in the lung is of a chronic inflammatory type also. It is compressed, very poorly expanded, shows a diffuse growth of new fibrous tissue, many nodular collections of lymphocytes, and, very rarely, a giant cell. In some ways, therefore, there is a resemblance to tuberculosis, but endothelial cells and tubercles are extremely infrequent compared to the extent of the infiltration. It is possible that tuberculosis and syphilis may exist here together.

The peribronchial nodes which are included in the sclerotic tissue show almost complete obliteration of normal structure, only a portion of the peripheral sinus and a small amount of the lymphoid

tissue remaining. One giant cell, about which are scattered a few endothelial cells, was found in one of these portions of nodes. This lesion does not justify a diagnosis of tuberculosis, for the absence of caseation and the replacement of the rest of the node with the dense sclerotic material suggest rather a syphilitic granuloma. Other nodes are deeply anthracotic and show diffuse hyaline deposits along the course of the reticulum.

The cardiac muscle shows some atrophy throughout, but the only inflammatory change is a very slight round-cell infiltration underneath the endocardium.

The liver cells are slightly atrophic, due to chronic passive congestion, and small foci of round-cell infiltration in the perilobular tissue are present. This is of uneven distribution and represents an early stage in a cirrhotic process. Productive inflammation is not seen.

The spleen shows also a well-marked chronic passive congestion, but little or no fibrosis.

A Levaditi stain of these tissues failed to show spirochetæ.

Literature. The clearest description of this condition is to be found in a short paper by Lian, published in 1913. The author believed that a fibroid tuberculous mediastinitis attacks the inferior mediastinum, and that even the rapidly caseating forms with abscess formation, which may originate in the superior mediastinum, usually follow down the fascial planes and present inferiorly on the pericardial surface. Syphilis, on the other hand, is a disease of the superior mediastinum. A third diffuse form involving both is very rarely seen. In the syphilitic cases three types are described: the respiratory, which is characterized by inspiratory dyspnea, a whistling stertorous type of respiration, rapid, diminished breath sounds, substernal retraction, cyanosis without edema, and attacks of suffocation due to pressure on the recurrent nerves. In the superior vena cava type, which, it is generally agreed, is the most frequent one, the symptoms are almost entirely circulatory and respiration is difficult only on effort. Precordial pain, tachycardia, headache and epistaxis are seen, and cyanosis, which may be very intense or which may be present only when stooping over. The edema may be limited to the eyelids, conjunctivæ, parotid and supraclavicular regions.

Osler also gave considerable attention to the subject of superior vena cava thrombosis, collecting 29 cases. He differentiated between the clinical pictures produced by thromboses of each of the three great veins, describing the type of superficial venous dilatation characteristic of each. The venous dilatation of the superior type is chiefly vertical and appears in the eyelids and over the root of the neck and the first rib where prominent, parallel veins appear at right angles to the line of the rib. A connection is established with the perforating branches of the internal mammary veins. The anastomoses with the superficial epigastric veins take

place down the front of the thorax, and to a much less extent by way of the veins around the umbilicus and xiphoid. This may be differentiated from the picture in cases where the inferior vena cava is obstructed. A patient with this type of obstruction presents on the lateral chest walls enlarged thoraco-epigastric veins which enter the apex of the axillæ, anastomosing in the iliac regions with branches of the superficial epigastric veins. In portal obstruction the axillary trunks and parasternal branches are large, but the greatest dilatation is over the region of the diaphragm. Osler states that complete thrombosis of any one of these three veins may exist for years with reasonably good health and freedom from discomfort.

More lately Howard has taken a somewhat different view from that of the French writers regarding the etiology, believing that most of the cases are tuberculous, and only a small proportion syphilitic. He described in 1915 2 nonfatal cases, 1 of which had a long duration, seven years, with very marked dyspnea and cyanosis, hemoptysis and cough. Improvement occurred and was thought to be due to a regression and healing of the tuberculous process. Howard's second case is of the inferior mediastinal type, with adhesions, pericardial and pleural, due to empyema and possibly pericarditis.

The French writers, however, maintain the importance of syphilis as a factor, and Lian's paper is obviously the result of their observations.

The case of Comby is one of the few in which the clinical findings were substantiated by autopsy. In 1892 the patient was seen first with signs of obliteration of the superior vena cava and attacks of suffocation and retrosternal oppression. Syphilis had been present for six years and had been practically untreated. The symptoms were alarming; extreme congestion of the face, defective sight and hearing, headache, epistaxis and attacks of dyspnea with cyanosis. Under mercurial treatment the symptoms subsided, but coincident with this improvement there developed an anastomotic circulation which remained very obvious for seven years. The patient died in 1906 of general paralysis, and at autopsy the anterior mediastinum was filled with a mass of fibro-adipose tissue tightly adherent to the trachea, bronchi, and great vessels, especially the superior vena cava.

Sebillotte in a thesis published in 1912 analyzes 31 case records, but few are complete from the pathological standpoint. The author mentions syphilis as the chief agent and thinks that the original lesion may be a syphiloma of the trachea or of one of the bronchi. The terminal state of such a lesion is seen in such a specimen as was taken at autopsy from the case of Brander and Holroyd, but the early stages are rarely seen.

Renault in 1913 reviewed the subject and described a case which clearly belongs in this group clinically, though pathologically we

must reserve some doubt. The patient was a woman, aged thirty years. In 1909 she had pain in the anterior part of the thorax and sense of oppression. At times she suffered much pain and was cyanosed, with alternate aphonia and dysphonia. The symptoms were improved by medication with iodids, but in 1912 again appeared. Dyspnea became very severe and asthmatic attacks frequent, the thorax painful, dysphonia intermittent. The radiogram showed a heavy shadow in the mediastinum and the Wassermann test was positive. The symptoms again greatly improved under treatment with iodids, mercury and arsphenamine.

Others, as Blankenhorn, believe the obstructive respiratory types, which resemble the bronchial asthma cases, to be due to syphilis of the large vessels, usually the aorta, but occasionally the vena cava. Blankenhorn mentions, also, as most writers do not, the peculiarly varied character of the symptoms—the paroxysmal change in pulse rate and respiration, the sudden changes in lung volume, the laryngeal crises and bi-tonal voice or aphonia—a picture which is well shown in the writer's case.

We are indebted to Harris for the most complete survey yet made of mediastinal conditions as a whole, and while present methods of diagnosis would undoubtedly change some of his tabulations, they are, in general, no doubt very accurately made. Of the 185 cases which this author studied, he was able to find only a small group of chronic nonsuppurative inflammatory cases, and of these but one is of the type under consideration. It is described by him as "characteristic mediastinitis proper." There was "excessive fibroid induration of the upper pleuræ and lungs with matting in the upper mediastinum suggesting tumor, also apical tuberculosis with cavitation and extensive pleurisy. The pericardium was not affected."

Many cases characterized by progressively increasing dyspnea and cachexia, even when syphilis is known to be present, do not justify a diagnosis of mediastinitis, for in these a tumor or an aneurysm has been found at autopsy much more often than the fibrotic lesion of the fascia alone. Davis, however, reported with autopsy findings a lesion closely resembling the one under consideration, but with complete obliteration of the superior vena cava, due to an old thrombosis and periphlebitis.

Diagnosis. A study of the literature of the subject shows, therefore, that a diagnosis has most frequently been made solely upon clinical grounds—with perhaps a corroborative positive Wassermann reaction in the more recent cases—but often the therapeutic test has been the sole dependable basis for establishing a differential diagnosis. The older cases cited show that this has been given the weight of evidence most often, but we cannot overlook the fact that many cases of mediastinal pressure are yearly seen upon which an accurate diagnosis is never made. If the therapeutic test of mercury and iodids fails in a late stage of the disease, the

fact offers not even negative evidence, for a mass so avascular, so extensively fibrotic and hyaline and so unabsorbable, such as this tumor is, could not be expected to be influenced particularly by medication. Even careful clinical observation may leave a margin of doubt as to whether syphilis is the sole cause or merely coincident; whether it has damaged primarily the coronary vessels and so the myocardium, or whether the obstruction is just above the heart. Difficult to differentiate also may be a severe syphilitic degeneration with the peculiar type of cyanosis, dyspnea, and secondary polycythemia described by Ayerza and later by Warthin. It is also difficult to determine whether the aorta or one of its larger branches is the principal site of damage. Multiple small aneurysms have frequently been seen in the aortic arch, which if they happen to protrude in the antero-posterior plane without a noticeably widened arch, arouse little clinical interest. A thymus large enough to be of clinical importance is a great rarity after childhood, and it is rather the tumors of this gland which are entitled to serious consideration in adults. A substernal aberrant thyroid has been seen but not with sufficient frequency to permit of probable diagnosis. Enlarged tuberculous lymph nodes are of course by no means rare and in some cases, as in this and in Howard's, probably such a cause cannot be excluded. Hemoptysis has occurred in both diseases. The productive or granulomatous pneumonia of syphilis usually affects the lower lobes most prominently. The pneumothorax at first glance suggests tuberculosis, but with extreme dyspnea and emphysema it may occur in other diseases. Hodgkin's disease and lymphosarcoma are often primary in the mediastinal nodes, but so frequently do they involve the cervical or axillary chains that confirmatory evidence is usually obtained in this way and a diagnosis of these diseases is rarely considered conclusive at present unless it is made from examination of excised tissue. Other types of malignant disease, as the small cell or other widely infiltrating types of carcinomata from a latent tumor of stomach, bile ducts, or breast, may so closely simulate syphilitic mediastinitis as to require considerable time and observation to make a diagnosis. The trachea, bronchi and recurrent nerves may be to the same extent embedded in dense sclerotic tissue and respiration become equally difficult.

Of the 29 cases of superior vena cava obstruction collected by Osler, 7 were found to be due to syphilis, and only 1 to carcinoma. Another series might give a different proportion, but syphilis must be a relatively frequent cause.

It is well to remember that treatment to be effectual must be begun early before destructive or sclerotic processes have proceeded beyond the point of repair.

An asthmatic etiology may generally be determined or eliminated by careful observation of the symptoms. In our patient the early

appearance and persistence of dysphagia, the hemoptysis, the inspiratory type of dyspnea, all suggested at once some other cause than foreign protein sensitization. The latter principle, while offering new and fascinating explanations for many obscure conditions, should not divert us from anatomical lesions, and no consideration of monkey fur or the proximity of rodents divert us from thorough physical examinations and precise observations.

Conclusions. A case of chronic mediastinitis causing the death of a young colored woman is described.

Syphilis is believed to be the etiological factor.

The lesion is a dense hyaline connective tissue mass, with granulomatous areas, sclerosing and constricting bloodvessels, nerves and the large bronchi. The infiltration and productive inflammation closely simulate in extent and effect a malignant tumor.

BIBLIOGRAPHY.

Allbutt and Rolleston: System of Medicine, 1909, **5**, 612.
Blankenhorn: Affections of Mediastinum, Nelson's System of Medicine, New York, 1920, **3**, 576.
Brander and Holroyd: Lancet, 1911, **2**, 1766.
Carrera: Am. Jour. Syphil., 1920, **4**, 1.
Comby: Bull. et mém. Soc. méd. d. hôp., 1892, **9**, 5; 1893, **10**, 859.
Comby, Vigouroux, et Collet: Bull. et mém. Soc. méd. d. hôp., 1906, **23**, 136.
Davies: Lancet, 1911, **2**, 1345.
Harris, T.: Indurative Mediastino-Pericarditis, London, 1895.
Habershon: Trans. Path. Soc., London, 1876, **27**, 79.
Howard: Bull. Johns Hopkins Hosp., 1915, **26**, 140.
Lian: Med. Press. and Circ., London, 1913, **96**, 143.
McLester: The Oxford Medicine, 1920, **2**, 210.
Osler: Bull. Johns Hopkins Hosp., 1903, **14**, 169.
Oulmont et Delort: Bull. et mém. Soc. méd. d. hôp., 1912, **33**, 793.
Phillips: Jour. Am. Med. Assn., 1922, **78**, 1355.
Renault: La mediastinite syphilitique, Thèse, Paris, 1912–1913.
Sebillotte: Thèse, Paris, 1912.
Siebert: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1913, **26**, 843.
Sorel, H. E.: Province méd., Lyon, 1913, **26**, 182.
Warthin: Am. Jour. Syphil., 1917, **1**, 693.
Wilks: Guy's Hosp. Repts., 1871, **16**, 196.

PRIMARY TUBERCULOUS PERICARDITIS, WITH REPORT OF A CASE.

By William B. Rawls, M.D.,
NEW YORK.

According to the literature, secondary tuberculous pericarditis is a fairly common disease but primary tuberculous pericarditis (in the pathologic as well as the clinical sense) is very rare. Hedblom, in a review of all the literature in 1921, found only 13 cases proved by necropsy. Because of this rarity, I believe it worth while to add another case report to the literature.

Case Report. (Hospital No. 164926.) A male negro, aged fifty-one years, was admitted to the hospital, May 27, 1924, complaining of (*a*) pain over the heart, (*b*) shortness of breath, (*c*) constant vomiting and (*d*) swelling of the feet. There was no history of tuberculosis in the family, and his past history was unimportant in reference to present illness. Syphilis was denied.

He was well and working every day until four months ago (January 20, 1924), when he began to tire easily and was short of breath on doing his customary work. At this time there was no swelling of the feet and no cough. The shortness of breath gradually increased, and three months later it was so severe that he was forced to quit work and go to bed. At this time he began to have dull aching pain over the heart, which was constant and did not radiate. He also noticed that on retiring at night his feet were swollen, but the swelling would disappear during the night. He now also began to have a dry and nonproductive cough. These symptoms persisted, gradually growing worse until he entered the hospital one month later. One week before entrance to the hospital he began to vomit. At first he vomited only two or three times daily, but vomiting became more frequent until date of admission, when he was vomiting almost constantly.

Physical examination revealed orthopnea, anxious expression and marked dyspnea, which was increased on the slightest exertion. The pupils were equal and reacted to light and accommodation. Deep reflexes were present and apparently normal. Lungs: There was evidence of consolidation over the lower left lobe posteriorly and congestion of the right lower and middle lobes posteriorly, as shown by the following physical signs: Expansion was poor and limited on the left. Tactile fremitus was increased over the lower right lobe posteriorly, but was absent over the lower left lobe posteriorly. There was dulness on percussion over the lower left lobe posteriorly and decreased resonance over the lower right lobe posteriorly. There was an absence of the breath sounds from the angle of the left scapula downward and suppression of breath sounds over the lower right lobe posteriorly. There were numerous small mucous rales over the right lung posteriorly up to the angle of the scapula and anteriorly to the fourth rib, and in the infrascapula region on the left. Heart: There was no palpable thrill at the apex, and the apex beat was not felt. On percussion the area of cardiac dulness extended to the left to the posterior axillary line, downward to the sixth interspace and to the right 5 cm. from the midsternal line. On turning the patient from side to side there was a shifting in the area of cardiac dulness. The heart sounds were very weak and distant, and were barely heard with a stethoscope. No murmurs were present. The apex rate was 130 per minute, extrasystoles were present (20 out of every 130 beats), but there was no pulse deficit. Abdomen: The liver was enlarged

about 6 cm. below the costal margin in the midclavicular line and was tender on palpation; there was no evidence of ascites, but there was marked edema of the lower extremities. The urine showed a strong trace of albumin. The blood Wassermann test was negative. The patient was given digalen, 20 min., intravenously every six hours without apparent improvement. On May 29, thirty-six hours after admission, 600 cc of turbid hemorrhagic fluid, with a large amount of fibrin floating free in the fluid, was withdrawn from the pericardial sac by the substernal route. He was slightly improved following this aspiration, and on May 31 400 cc of the same type of fluid was again withdrawn, and the same amount of air injected into the pericardial cavity, but the patient died eight hours later. Culture on both specimens of fluid were negative after forty-eight hours' incubation. A guinea pig was injected with the pericardial fluid and necropsy on guinea pig six weeks later revealed miliary tubercles in the spleen, liver and lungs and an enlargement of the mesenteric lymph glands. A smear from macerated enlarged mesenteric lymph gland of the guinea pig showed tubercle bacilli present.

Necropsy: The following is an extract from the necropsy report: There was marked congestion of the lower lobe of the right lung. *The lymph nodes at the hilus of the lungs and of the thoracic cavity were not enlarged and showed no evidence of tuberculosis.* The lower lobe of the left lung was collapsed due to pressure from the heart. *On section of the lungs there were no calcified areas and no evidence of tuberculosis. The cervical and thoracic vertebræ showed no evidence of tuberculosis.* Heart: The pericardial sac occupied almost the entire left pleural cavity, extending 17 cm. to the left in the fifth interspace and 7 cm. to the right in the fourth interspace. On section of the pericardium it was seen to contain an abnormal amount of turbid hemorrhagic fluid. There was a marked proliferative pericarditis, both the fibrous and serous coats being much thickened and laminated, varying in places from $\frac{1}{4}$ to $\frac{3}{4}$ inch. The inner surface of the pericardium and epicardium was covered by a large amount of granulation tissue, to which adhered pedunculated masses of partially organized tissue. Some of these masses formed adhesions between the layers, imperfectly dividing the cavity into lesser cavities which contained turbid hemorrhagic fluid. The walls of the left ventricle were concentrically hypertrophied. The weight of the heart was 180 gm. The cavity of the left ventricle was small. The endocardium was smooth and glistening, and the valves were normal. The liver showed marked chronic passive congestion, with no evidence of tuberculosis. The spleen and kidneys were negative for tuberculosis. Mesenteric lymph glands were not enlarged and apparently normal. The mucosa of the intestine was smooth, with no evidence of ulceration; Peyer's glands apparently normal. The mucosa of the bladder was

normal; the prostate was enlarged, but on section showed no evidence of tuberculosis. There was no evidence of tuberculosis in any other part of the body.

Discussion and Summary. The above case was considered as one of primary tuberculous pericarditis; that is, it was proven to be tuberculous and clinically and pathologically it appeared to be primary, as no other focus of tuberculosis was found after careful search. The diagnosis was based on the chronicity, the presence of a relative large sterile effusion, guinea-pig injection and necropsy findings. Judging from the relative frequency at necropsy of pericarditis with adhesions of probable tuberculous origin in patients who have died of another disease, it is probable that a large proportion of patients with tuberculous pericarditis recover spontaneously. However, most patients with a large amount of effusion run a chronic course and die. The fluid reaccumulates; open drainage is followed by infection and the disease runs a characteristically downward course. In cases of secondary tuberculous pericarditis the course seems largely determined by the type and location of the primary lesion. In reference to the treatment, Weil, Wenckebach, Loiseleur and Oppenheimer have produced pneumopericardium with gratifying results, and concluded that the benefit derived is due directly to the effect of the air on the disease in a manner similar to the reputed effect of air on peritoneal tuberculosis. Postmortem statistics indicate that few disease processes are so frequently overlooked as those which effect the pericardium.

BIBLIOGRAPHY.

1. Hedblom: Surg. Clin. North America, 1921, **1**, 1411.
2. Weil, P. E., and Loiseleur: Insufflation d'air dans Pericardite tuberculeuse avec épanchement pneumopericardite et hydropneumopericardite artificiel, Presse méd., 1916, **24**, 601.
3. Oppenheimer, R. H.: Therapeutic Pneumopericardium in Pericarditis with Effusion, Jour. Am. Med. Assn., 1924, **82**, 1685.
4. Wenckebach, K. F.: Beobachtungen bei exsudativer und adhäsiver Perikarditis, Ztschr. f. klin. Med., 1910, **71**, 402.
5. Berard, L., and Pehu, M.: Pericardite tuberculeuse cliniquement primitive à grand épanchement sero-hematique; ponction pericardiotomie, Lyon méd., 1906, **196**, 678.
6. Mareceaux, M.: Un cas de pericardite tuberculeuse primitive, Jour. sc. med. de Lille, 1908, **2**, 165.
7. Riesman, D.: Primary Tuberculosis of the Pericardium, Am. Jour. Med. Sci., 1901, **122**, 6.
8. Scagliosi: Isolierte tuberkulose Pericarditis, Deutsch. med. Wchnschr., 1904, **30**, 873.
9. Virchow, R.: Ueber einen Fall von isolierter primarer tuberkuloser Perikarditis, Berl. klin. Wchnschr., 1892, **29**, 1315.

LYMPHATIC LEUKEMIA IN INFANCY WITH THE REPORT OF A CASE.

By Martha Wollstein, M.D.,

and

Frederick H. Bartlett, M.D.

(From the Babies' Hospital, New York.)

The Babies' Hospital records show a total of 25,246 admissions. Fourteen instances of acute lymphatic leukemia and one of acute myelogenous leukemia are included in this number. Few patients over three years of age are admitted to the hospital. The age of the infants with lymphatic leukemia ranged between ten months and four years. The age of the only case of myelogenous leukemia was two and a half years.

The patient who furnishes the occasion for this report was a girl who died at fourteen months of age. The unusually interesting autopsy findings and the comparative rarity of lymphatic leukemia in infants of this age have led to a detailed report of the case.

Clinical Course of the Disease. G. F., aged twelve and a half months, was admitted to the hospital, March 17, 1924. The parents said she had been listless and pale for about three weeks, and breathing rapidly for two days before admission. There was no history of angina. Neither the family nor the birth history has any bearing on the case. She had always been well nourished. The present illness began with lessened activity and a gradually lessening desire to play. At the same time the mother noticed that the baby had been growing pale. The occasion for bringing her to the hospital was the sudden appearance of rapid breathing associated with extreme weakness, so that the child was in a condition resembling collapse when admitted.

Physical Examination. The baby looked acutely ill. The skin was bloodless, as were the mucous membranes. The breathing was rapid, regular and shallow.

Skin. There were scattered areas of bluish discoloration, but no definite petechial spots.

Abdomen. The abdomen was distended. The liver edge was felt 11.5 cm. below the costal margin and the spleen 9 cm. below. There was neither rigidity nor tenderness.

Mouth. The tonsils were moderately enlarged.

There were no other abnormal findings in any organs. The diagnosis made by the admitting physician was as follows: Acidosis; leukemia or aplastic anemia.

Course of the Disease in the Hospital. *March* 18. Because of the obvious anemia, confirmed by a blood count showing 824,000 red

cells per cu.mm. and 20 per cent hemoglobin, the child was transfused by the direct method with 190 cc of blood from the mother. Before transfusion the differential count showed 5 per cent polymorphonuclear neutrophiles, 93 per cent lymphocytes, and 2 per cent basophiles. Six nucleated red cells were counted to 100 leukocytes. The blood platelets numbered 152,000 per cu.mm. The absolute number of mononuclear cells was 53,163, and of polymorphonuclears 3,997, while the normal numbers should have been 34,260 and 22,840 per cu.mm.

March 19. After the transfusion a few petechial spots were noticed over the posterior sufrace of both legs, more numerous on the right.

March 24. The child seemed much improved. There was no change in the size of the liver and spleen. Two pale blue areas were noticed on the skin over the back.

March 28. A small hemorrhagic vesicle appeared on the chin just below the lip. It was surrounded by ecchymoses, and the spot looked like a blueberry.

March 29. The child was given a transfusion of 160 cc of the mother's blood by the direct method.

April 3. The crust which had formed over the spot on the chin fell off, leaving a raw surface. A similar spot appeared on the left cheek. Another transfusion of 140 cc of the mother's blood was given by the direct method.

April 7. The baby took food well and was holding her weight, giving the impression of slight improvement.

April 8. Tryparsamide,[1] 0.35 gm., was injected intramuscularly into the buttock for its tonic or catalytic effect.

April 11. The general condition showed distinct improvement. The liver and spleen remained practically unchanged in size.

April 13. The patient was discharged because of her improvement, with instructions that she be carefully watched.

April 17. The child was brought for tryparsamide injection and blood examination. She showed a gain in weight from 7,270 to 7,580 gm. and a gain in the number or red cells and hemoglobin, both of which reached the high mark for the time of observation. This was fourteen days after her third transfusion.

April 25. She returned for treatment and again showed a gain in weight. However, the hemoglobin, the red cells and the leukocytes were all diminished and there were purpuric spots on the legs. Inguinal, axillary and epitrochlear lymph nodes were enlarged and the abdomen was distended. In the anterior axillary line the spleen reached 10 cm. below the costal margin and in the mid-axillary line the liver extended 10 cm. below. Readmission was advised because the child was evidently losing ground. Death occurred in the hospital on May 5.

Throughout the entire course of the disease, the urine had not shown anything abnormal.

The temperature was irregular in type. During the first two weeks in the hospital, it ranged between 100 and 103° F. After the first transfusion it reached 104° F. During the next two weeks it was lower, from 98 to 100° F., rising again to 101° and 102° F. during the week before she died and reaching 104.8° F. on the morning of her death.

Summary of Clinical Features. Marked pallor, rapid breathing with extreme weakness, fever, ecchymoses and petechial spots on the skin, enlargement of the liver and spleen, temporary improvement in the general condition following transfusions, then the rapid and progressive decline resulting in death mark the clinical course. The duration of the disease from the observation of the first symptoms to death was a week more than two months.

Discussion of Blood Findings. The red blood cells were lowest on admission (824,000 per cu.mm.). They rose after the first transfusion to 2,200,000, but fell back in eight days to 1,500,000. They rose again, after the second transfusion, to 2,224,000 and after the third transfusion increased steadily for two weeks to 3,184,000. After that the red cells declined in a week to 2,400,000 per cu.mm.

The hemoglobin ranged between 19 and 70 per cent, and the color index from 1.25 to 1, which is rather high. Vogel[2] found both high and low indices in his series of leukemia patients. Naegeli[3] found the index regularly high in lymphatic leukemia.

The leukocyte count on admission was 57,000 per cu.mm. and on the next day it had fallen to 10,000. The count gradually dropped to 2050 on April 3. During this time, March 18 to April 3, the child received three transfusions. Nevertheless the leukocytes steadily dropped, which is important and significant as indicating that the transfusions had no apparent effect in stimulating the production of white blood cells.

The striking phenomena in the white count are: the total of 57,000 leukocytes on admission and the drop to 10,000 cells on the next day; the leukopenia, reaching a minimum of 2050, during most of her stay in the hospital; the terminal increase to 21,150 leukocytes on the day she died.

It is important to emphasize the point that acute lymphatic leukemia in infants may coexist with leukopenia, which leukopenia may be present during the greater part of the disease. In this instance, it lasted for one month, from March 24 to April 25. For a period of three weeks, tryparsamide was administered intramuscularly for its possible catalytic effect,[4] in doses of 0.05 per kg. of body weight. Whether a sufficient amount of the drug had been given to affect the blood is open to question. It must be taken into consideration, however.

Necropsy Findings. G. F., aged fourteen months. May 5, 1924. An abdominal incision only was permitted. The body was that of an emaciated, white female infant. There were purpuric spots

on the skin of the face, chest, abdomen and lower extremities. The abdomen was distended. The superficial cervical lymph nodes, the inguinal and axillary nodes were symmetrically enlarged.

Liver. It weighed 875 gm. and extended 6 cm. below the lower border of the sternum and 7.5 cm. below the margin of the ribs in the mammary line. The transverse diameter measured 20 cm. and the right lobe measured 15 cm. anteroposteriorly. The capsule was smooth. On the surface and in the substance there were many round white areas, 1 to 2 mm. in diameter. These were surrounded by a narrow zone of congestion, giving a mottled red and yellow appearance (Fig. 1). On section the liver substance showed some fatty change and many leukemic nodules. In the transverse fissure

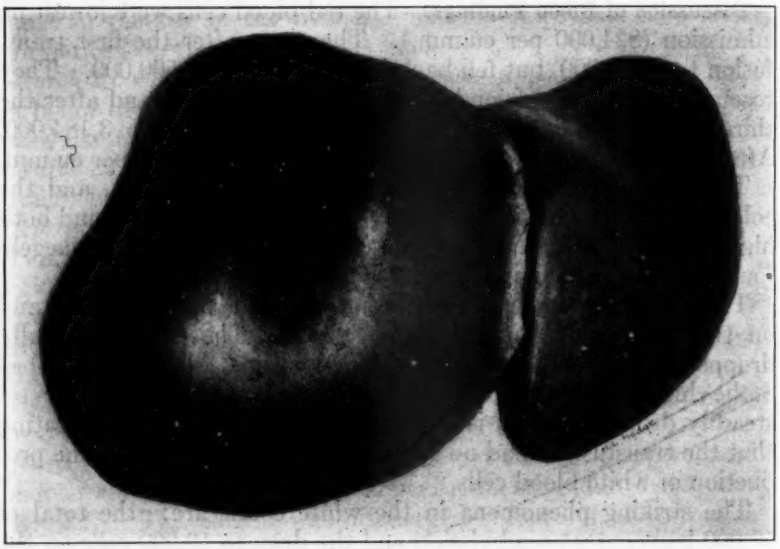


FIG. 1.—Liver showing leukemic nodules surrounded by zones of congestion.

there were several large lymph nodes. One of these measured 1 cm. in diameter and was hemorrhagic in its upper half, but pale in the lower portion.

The *spleen* extended to the upper border of the ilium, weighed 212 gm., and measured 12.5 by 8 cm. The capsule was smooth. There were a few subcapsular hemorrhages apparent (Fig. 2). The substance was rather soft. On section there were many small white nodules 1 to 2 mm. in diameter. In the hilus of the spleen there was a lymph node, 5 by 9 mm. in diameter.

The *stomach* was distended with food and also contained a small amount of blood-stained mucus. The mucosa showed many hemorrhages, some linear and some 1 to 2 mm. in diameter. There were no ulcers.

The *pancreas* was normal and firm in consistency. It showed many capillary hemorrhages beneath the capsule and into the substance. The lymph nodes along the upper border were markedly enlarged, dark red and 1.5 cm. long. On section they were fairly firm and had a smooth uniform appearance.

Intestines. The duodenum was normal. The jejunum showed visible solitary lymph nodes and small pinpoint hemorrhages in the mucosa. The Peyer's patches were not enlarged but they all showed small hemorrhagic areas. Just above the ileocecal valve

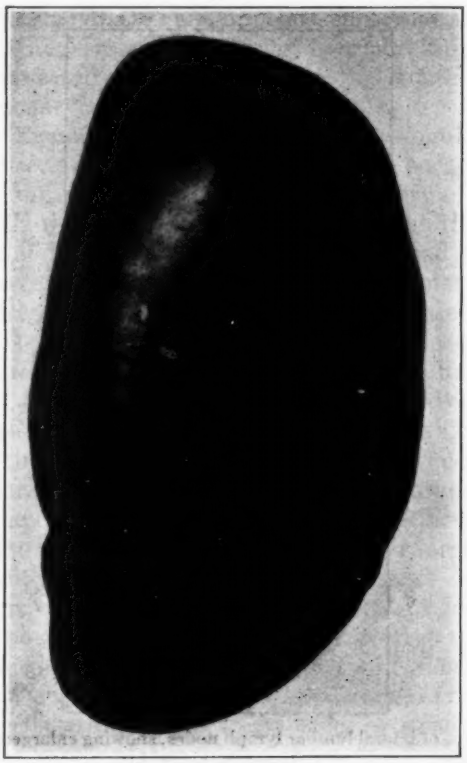


FIG. 2.—Spleen, greatly enlarged; deep red in color with subcapsular hemorrhages.

the follicles in a Peyer's patch were distinctly hyperplastic and red in color. In the large intestine, the solitary follicles were all slightly enlarged and hemorrhages into the mucosa were numerous. There were no ulcers in the intestinal tract.

The *kidneys* weighed 100 gm. and were large, pale, moist and firm. Leukemic nodules were present in the boundary zone and in the medulla. Several of the nodules were 3 mm. in diameter. Hemorrhages varied from 1 to 3 mm. in diameter. The markings were blurred.

The *suprarenals* weighed 3 gm. They were pale yellow and showed a narrow medulla.

Heart. The muscle was flabby. Subpericardial hemorrhages were present. On the surface of the aorta, there were a few small lymph nodes, the size of a pin head. The valves were quite normal. There were no leukemic nodules to be seen.

Lungs. There was no pleurisy. The left lung was emphysematous throughout the upper lobe, and the posterior portion of the lower lobe contained a hemorrhage 5 cm. in diameter, less in depth. The right lung was emphysematous in its anterior two-thirds.

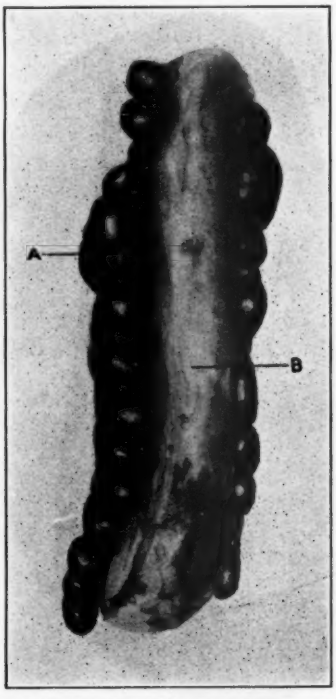


FIG. 3.—Chains of lateral lumbar lymph nodes, showing enlargement and hemorrhage, *a*; aorta, *b*.

Posteriorly the lower lobe contained a small atelectatic area, and the upper lobe an area of acute bronchopenumonia 2.5 by 2 cm. in diameter. Edema of both lungs was marked.

Lymph Nodes. The bronchial lymph nodes were all large and red in color. At the bifurcation of the trachea, the largest node measured 2.5 cm. transversely and 2 cm. vertically. On section small hemorrhages were apparent in the nodes. The substance was uniformly smooth, rather firm and very moist. A chain of lymph nodes along the aorta on both sides varied in size from 0.5 cm. to 1 cm. and in color from bright to deep red (Fig. 3).

All the abdominal lymph nodes were much enlarged, and pale red. The largest were just within the inguinal ring, where, on the right side, there was a dark red packet, 3.5 cm. in diameter, consisting of five nodes. Lying on the vertebral column was a chain of enlarged glands, many 1 cm. in length. On section, most of these glands contained hemorrhages.

Thymus. The gland was removed piecemeal and was apparently not enlarged. It was pale in color.

Bladder. The wall was very pale and contained many punctate hemorrhages into the mucosa.

Anatomical Diagnosis. Subcutaneous, subserous and submucous hemorrhages. Leukemic infiltration of liver and kidneys. Hyperplasia of spleen and lymph nodes (general). Acute bronchopneumonia. Pulmonary emphysema and edema.

Microscopic Examination. *Liver.* The liver lobules were small because collections of round, mononuclear cells occupied the interlobular areas and encroached upon the periphery of every lobule. The round cells were present within and without the intralobular and interlobular bloodvessels, which also contained red blood cells and a few larger mononuclear cells with vesicular nuclei. The Kupffer cells were distinct and in some places contained phagocyted fragments. No fibrous connective tissue was seen. Such liver cells as remained were narrower than normal and many contained large drops of fat. The bile ducts and the bloodvessels lay surrounded by masses of small, mononuclear cells. As a consequence of the cellularly infiltrated periphery and the fatty central portion, no lobule in the section presented a normal appearance.

Spleen. The connective tissue septa were distinct and were not increased in size nor in number. Both small and large bloodvessels were filled with red cells. Small hemorrhages had occurred. Brown pigment was present in small amounts. A few Malpighian bodies could be made out with a normal central vessel, but the periphery shaded into the surrounding mass of mononuclear cells. Consequently the splenic pulp had the appearance of a mass of small, mononuclear cells with congested capillaries between them.

Lung. The vessels of the pleura were filled with blood cells. Intrapleural and subpleural hemorrhages were present. Some alveoli contained only red blood cells, while others contained only serum. The contents of other alveolar groups were polymorphonuclear leukocytes, which also infiltrated the alveolar walls. Fibrine was present in small amount in these alveoli. The lesion was one of edema, hemorrhage and early bronchopneumonia.

Bronchial Lymph Node. In the greater part of the node, the cortex and the medulla could not be distinguished because there was diffuse mononuclear cell packing of both. The connective tissue was normal in amount. Many lymph sinuses were packed with mononuclear cells, although some of the largest were almost

empty. No germ centers were present. Phagocytosis of pigment granules and nuclear fragments was going on by means of large cells within the sinuses. These large cells were very numerous and in some places contained an entire small cell besides pigment granules. The bloodvessel walls were quite normal.

Lymph Node No. 2. The lymph nodules at the periphery of the node and the strands in the center were outlined by areas of hemorrhage. The nodules themselves were closely packed with lymphoid cells. Hemorrhages had occurred into the periphery of neighboring follicles.

Heart Wall. The pericardium was normal. The bloodvessels between the muscle bundles contained many mononuclear cells, but there was no perivascular infiltration. The muscle cells were normal. There were no leukemic nodules in the section.

Aorta. The wall of the aorta and a cusp of the aortic valve were normal.

Suprarenal. The cells of the cortex had undergone granular degeneration and in some places especially in the glomerular zone, were lacking. The medulla was wide, congested and the seat of small hemorrhages. Within the bloodvessels were mononuclear cells.

Kidney. In the cortex there were many collections of mononuclear cells. These varied in size, and in some instances had replaced both tubules and glomeruli (Fig. 5). Practically every one of these cell groups contained one or more bloodvessels, small and normal in structure. The tubules of the cortex, both the convoluted and the arms of Henle's loops, showed marked pealing of their lining cells and contained granular material. The glomeruli were normal. There was no fibrous connective tissue increase. The collecting tubules were normal in size and in shape. Many of them contained granular or hyaline casts. In the wall of the kidney pelvis were many perivascular areas of mononuclear cells. The epithelial lining of the pelvic wall was normal. There were areas in the boundary zone where the mononuclear cell infiltration had become so diffuse that the appearance was that of adenoid tissue with straight tubules running through it.

Stomach. The lining epithelium and glands were normal. Between the glands there were collections of mononuclear cells. These were both larger and more numerous than is the case in the normal stomach. The other coats were edematous, but showed no cellular infiltration.

Microscopical Diagnosis. Acute lymphatic leukemia: leukemic infiltration of liver, fatty infiltration of liver; leukemic infiltration of spleen, kidneys, stomach mucosa, thoracic and abdominal lymph nodes; pulmonary edema; acute bronchopneumonia.

Discussion. The interest in this case centers about the diagnosis during life, in the light of the clinical symptoms, the course, the dura-

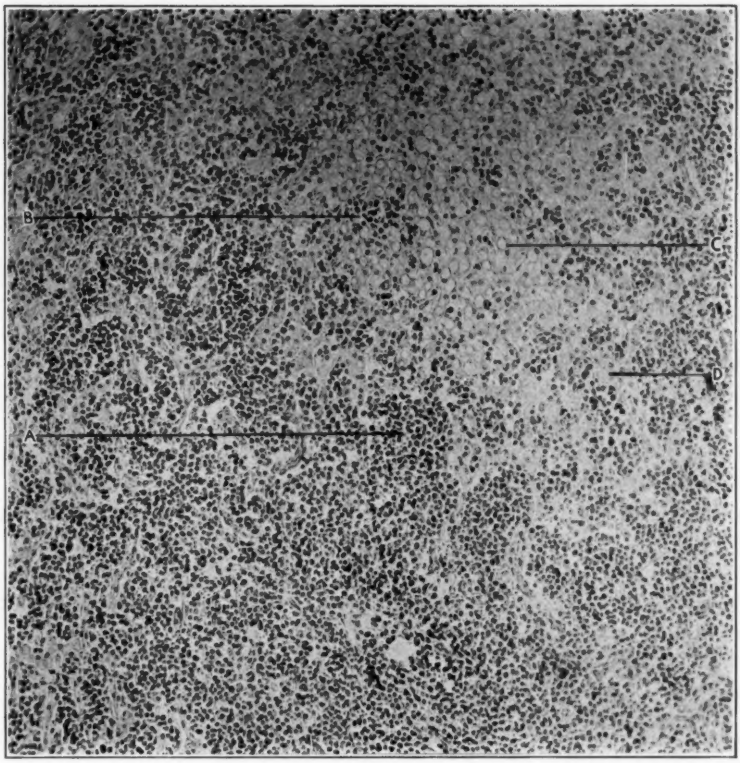


FIG. 4.—Liver, showing lymphocytic infiltration between (*a*) and within (*b*) the lobules; fatty liver cells (*c*); and normal liver cells (*d*).

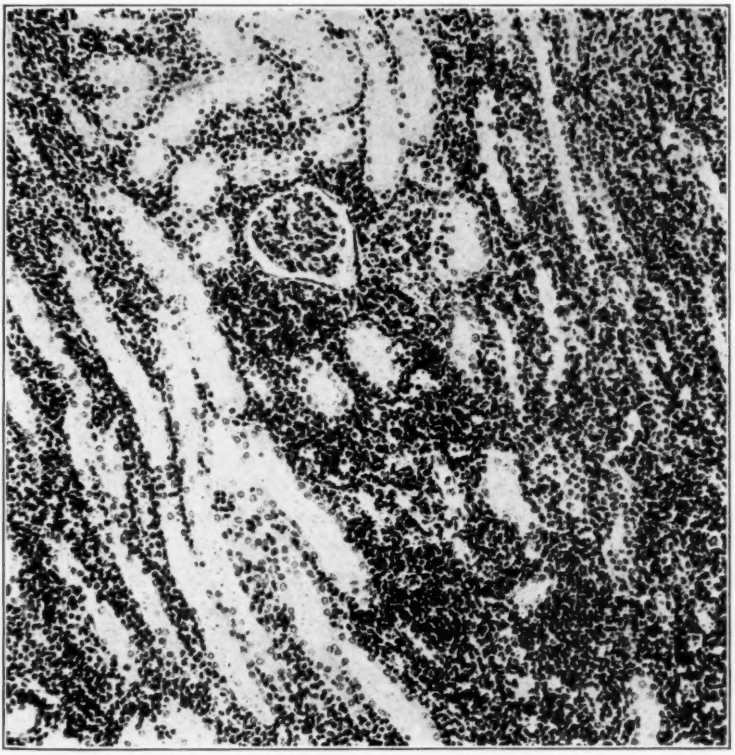


FIG. 5.—Kidney showing lymphocytic infiltration between the tubules and glomeruli.

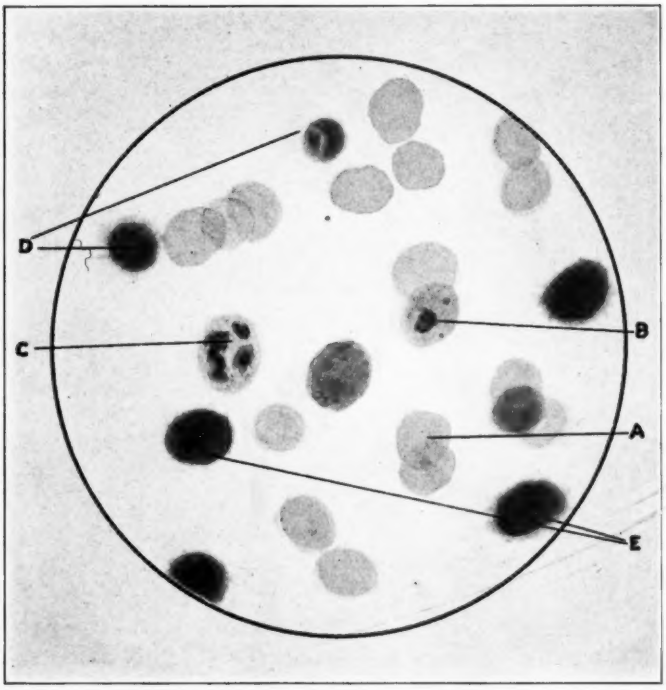


FIG. 6.—Smear of blood on March 18. *a*, red cell; *b*, normoblast; *c*, polymorphonuclear neutrophilic leukocyte; *d*, normal lymphocyte; *e*, pathologic lymphocyte.

tion and the blood picture. The postmortem diagnosis was apparent from the gross appearance of the liver, kidneys and lymph nodes, and was confirmed by microscopical sections of these organs.

The onset of the illness was characterized by gradually increasing pallor and listlessness over a period of three weeks, with sudden development of hyperpnea. This may have been due to diminished oxidation of the cells of the body. The cause of this, however, remains uncertain. The blood picture on admission suggested lymphatic leukemia because of the high number of leukocytes, the absolute preponderance of lymphocytes over granular cells and the reduction in the platelet count. Von Jaksch's anemia was excluded by the abnormally high number of lymphocytes, the comparatively few nucleated red cells and the absence of myelocytes from the blood, together with the absence of rickets, the presence of hemorrhages and the severity of the illness. The drop in the total number of leukocytes raised the question of whether we were dealing with an aleukemic stage of leukemia or with an aplastic anemia. The constant preponderance of the absolute number of lymphocytes over that of the polynuclear cells gave no aid, but the persistence of eight to ten nucleated red cells argued against aplasia. The hemorrhages from the mouth and the skin, and the rapidly downward course were in favor of leukemia. Aplastic anemia runs a much slower course and no case under one year of age has been recorded.

Transfusions were of only temporary help to red or white cells. That is, they either did not stimulate new blood formation, or they did not help to keep a normal number of cells in the peripheral blood.

The relative numbers of polymorphonuclear cells did increase after the first transfusion, and continued to do so for about one week, when a drop was apparent. After the second and third transfusions the polymorphonuclears increased again relatively, and more decidedly. Absolutely, however, the polymorphonuclear leukocytes never reached the number which is normal for the blood of a child of one year.

Among the cases of acute leukemia in infancy and childhood which have been reported, there are a number which show either an aleukemic stage or a completely aleukemic course. Baar[5] described 3 cases of his own and quoted extensively from the literature. In Baar's first case, which he looks upon as one of mixed lymphatic and myelogenous leukemia, the leukocytes fell as low as 2,000 per cu.mm. In the case of Hess and Isaac,[6] a boy aged three years, the leukocytes varied between 237,000 and 2000 in number. In our case the child came under observation with 57,000 leukocytes, which then rapidly fell to 2050 in spite of two transfusions. Before death the white cells had increased to 21,150. That the lymphocytes had been formed in much larger numbers than appeared in the

peripheral blood was shown by microscopical section of the kidney, liver and spleen. All these organs contained large collections of lymphocytes, evidently filtered out from the blood stream. Thus these cells in the circulating blood were decreased in number and the size of the viscera was increased.

The small mononuclear leukocyte which was the predominating cell in the blood from the first to the last day of the period of hospital observation, was round, with a nucleus which filled most of the cell body, contained a nucleolus and left a narrow cytoplasmic ring free from granules (Fig. 6.) The nucleus was often slightly indented. The resemblance to young myeloblasts was recognized, and the test for the oxidase reaction was made as a possible means of differentiation. The test proved to be uniformly negative, no granules being demonstrable in the cells under discussion, though the polymorphonuclear cells showed the dark blue granules characteristic of the reaction. The diagnosis of lymphatic rather than myelogenous leukemia then became certain, and was born out later by the microscopical examination of the organs. The absolute number of these mononuclear cells as compared with the polymorphonuclear elements was far in excess of the normal number for the child's age, and remained constantly so from first to last.

The platelets varied from 152,000 to 88,000 per cu.mm. being diminished throughout the period of observation.

We can see no point in designating a third variety of leukemia as due to "the large undifferentiated cell," as Wachi[7] has done. Realizing that the oxidase reaction may be absent from some myeloblasts, as Naegeli[3] has pointed out, we feel that only a tentative diagnosis can be made during life, and that the histology of the organs and marrow after death must be the final proof. Since, however, myelogenous leukemia is acknowledged to be exceedingly rare in infancy and even in early childhood, such a diagnosis will scarcely be accepted without postmortem confirmation, even should the oxidase reaction prove positive during life.

There are 14 cases on record at the hospital which were diagnosed as acute lymphatic leukemia on the blood findings, clinical symptoms, course and fatal outcome. Autopsies are lacking in all but two instances, chiefly because the patients died at home after being removed against advice. While we realize that if diagnosis of acute lymphatic leukemia in young children is to be unassailable, it must rest upon gross and microscopical study of the organs as well as upon clinical symptoms, there are nevertheless certain manifestations common to our 14 cases which will bear discussing.

There were only 2 girls, and 12 boys in the group. Minot and Isaacs[8] state that while leukemia is three times as common in males as in females, in the first years of life girls are relatively more often attacked than are boys. Thus the youngest of Baar's cases, the only one under two years of age, was a girl. Gautier and Thevenod[9]

report the case of a girl one year old. They also collected 7 cases reported since 1909, of whom 4 were boys. The youngest case observed at the Babies' Hospital was a boy, ten months old. Smith's[10] case occurred in a boy of six weeks.

It is noteworthy that rickets was absent from 11 of the 14 cases and that it was marked in only one child in the series. In no instance was a positive Wassermann reaction obtained. No child in the series recovered.

Hemorrhages were present in every case, and always into the skin, combined in some patients with bleeding from the mouth (gums or lips), nose, intestine, urinary tract or into the conjunctiva. Hemorrhage is an essential symptom of acute leukemia. In those cases in which platelets were counted, they were low in number.

The disease lasted from three weeks to five months. Morquio[11] says in this connection that in his cases the true leukemic phase was sometimes as short as a week, and that the preleukemic phase may last two to six months.

The red cells numbered from 500,000 to 3,000,000 in most of our cases. Only 4 patients had more than 3,000,000 red cells, and none had over 4,000,000 at any time during the course of the disease.

It is possible to group the cases according to the way the leukocytes varied. Thus, in 5 cases they decreased consistently, twice to a leukopenia (117,000 to 2500), three times remaining far above normal (123,000 to 55,000). In only 1 case did they consistently rise during the period of observation. Irregularities in the count occurred in 4 cases after transfusions and in 1 other after treatment with benzol. One case showed marked fluctuations in the number of leukocytes over a period of five months, with no therapeutic measure to explain the variations. The highest number recorded in this boy was 63,200 and the lowest 4500, the counts on successive days showing surprising differences. During an attack of otitis, the leukocytes remained in the neighborhood of 6000, but several months later, without any discoverable lesion, they rose from 15,000 to 60,000. Six cases showed an aleukemic stage of the blood during the period of observation, but only the one detailed in this paper ran an aleukemic course during the greater part of the duration of the leukemia.

The spleen was enlarged in every case in our series. In 5 children its lower border reached the iliac crest, while in 5 others it extended only 1 to 3 cm. below the costal border. In the other 4 it was 4 to 6 cm. below. The liver was enlarged to a moderate degree in 10 children, but in 4 others it reached the umbilicus.

The superficial lymph nodes were palpable in all these patients, usually noted as being the size of a small bean or shot. In one instance an axillary node was as large as a walnut. The nodes were always movable and discrete. In no instance were there any large deforming masses in the neck or elsewhere.

The onset was sudden in 7 cases, with fever and hemorrhage into the skin, accompanied by epistaxis in 4. The gradual onset in the other 7 children was marked by pallor, fatigue and anorexia accompanied once by abdominal pain and once (in the case of G. F.), by sudden development of hyperpnea.

In 2 cases which came to autopsy, the thymus was not enlarged. Rocaz[12] reported the case of a boy aged four years in whom acute lymphatic leukemia began with angina and proved fatal on the twenty-fifth day. The thymus gland weighed 200 gm.

Summary. A case of acute lymphatic leukemia in a female infant of fourteen months is recorded in clinical and anatomical detail.

An aleukemic phase of acute lymphatic leukemia in infants and young children is not uncommon. Consequently the diagnosis can only be made after repeated examination of the blood in conjunction with a study of the clinical symptoms and course.

Hemorrhage is an essential symptom of acute leukemia in infants, and the number of platelets is low throughout the disease.

Transfusions have only a temporary effect in raising the hemoglobin per cent, the number of the erythrocytes or the number of the leukocytes.

Macroscopical and microscopical leukemic nodules were found in the liver and kidney, while the spleen and lymph nodes showed diffuse infiltration with lymphocytes.

REFERENCES.

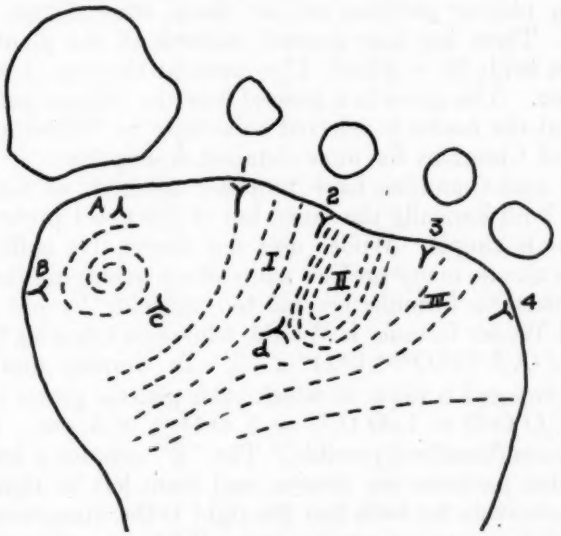
1. Jacobs and Heidelberger: Jour. Exp. Med., 1919, **30**, 411.
2. Vogel: Nelson's Loose Leaf Medicine, vol. iv, p. 66.
3. Naegeli: Blutkrankheiten und Blutdiagnostik, Berlin, 1923, 4th ed.
4. Brown and Pearce: Jour. Am. Med. Assn., 1924, **82**, 5.
5. Baar: Jahrb. f. Kinderh., 1924, **104**, 1.
6. Hess and Isaac: Monatschr. f. Kinderh., 1921, **21**, 442.
7. Wachi: Thèse de Paris, 1924.
8. Minot and Isaacs: Boston Med. and Surg. Jour., 1924, **116**, 1.
9. Gautier and Thevenod: Le Nourrisson, 1924, **12**, 1.
10. Smith: Am. Jour. Dis. Child., 1921, **21**, 163.
11. Morquio: Arch. Espan. Ped., 1923, **7**, 641 and 705.
12. Rocaz: Rev. Mens. Mal de l'Enfance., 1902, **20**, 120.

SOLE PRINTS OF NEWBORN BABIES.

By Robert B. Montgomery, B.S., M.D.,
MADISON, WIS.

For a number of years certain hospitals, both lying-in and general, have been taking sole prints of the newborn babies, but to the best of my knowledge no effort has been made to read and classify the patterns found. In most cases two sets of prints are

taken—one to be given to the parents and one to be placed in the baby's (or mother's) chart. The prints are usually taken by the smeary, black-ink method commonly used in taking finger prints, and are of little value, either for correctly reading the details of the patterns or for correctly establishing the identity of the baby, should such an occasion arise. It rarely happens, to be sure, that a woman doubts the identity of the baby given her by the hospital attaches. If she should, how can it be proved without a shadow of a doubt that it is hers, and if not, whose it is? The method described is not intended to replace the usual methods of identifying the baby, but to supplement them, and is simple enough to be used by anyone after a little instruction.



Illustrating use of the formulæ. Hallucal pattern is a whorl (*W*). First plantar pattern is an open field (*O*); second is open at the top (*U*); third is an open field (*O*); giving combination 5 according to Wilder's table. Only one lower delta (*d*) is seen. Formula: *W5d*.

Prof. J. H. Mathews, of the University of Wisconsin, has perfected a process which is, to my mind, far superior to ink in making either finger, palm or sole prints. The details of the process have not yet been made public, but will be in the near future. Ink has proved very satisfactory in finger-print work where the papillary ridges are very large, but the ridges on the sole of a newborn baby's foot are so small and so delicate that the ink is pushed between them and only an unintelligible smear results. Naturally, the details of the patterns cannot be made out, and the method defeats the purpose. On the other hand, the method used by Professor Mathews gives a print which looks like a fine etching.

The details can be readily seen under a glass of about six diameters' magnification.

When the prints have been prepared the next step is to look for the patterns on the ball of the foot, and to reduce the description of them to a formula. Space does not permit a detailed description of the various patterns and lines, but some of the essentials will be explained. There are two general areas to be considered: The hallucal (area back of the great toe) and the plantar (area back of the other toes). There are five patterns in the hallucal area, the open field (no pattern), the whorl and the others (A, B, C) which denote which delta is missing. A delta is found where three papillary ridges come together to form a "Y." There are four digital deltas also, and between them lie the three plantar patterns. Below the plantar patterns are, at times, other deltas, from one to three. There are four general patterns in the plantar areas: O = open field; W = whorl; U = open at the top; ∩ = open at the bottom. This gives in a general way the various patterns and deltas, and the reader is referred to articles by Wilder and Wentworth, and Cummins for more detailed descriptions.

Wilder and Cummins have proposed methods of formulation. They are both basically the same, but of the two I prefer Wilder's because it is simple. Wilder uses few descriptive suffixes, while Cummins uses so many prefixes and suffixes qualifying the primary symbols that his formulæ become too unwieldy for our purposes. A typical Wilder formula is W17dd, while one following Cummin's method is $(A)U^{1}O^{1t}.O^{s11d}.U^{3}.O^{4+}.2+3$. To simplify matters, Wilder has proposed a table in which each plantar group is given a number: O O O = 1, O O U = 2, O O ∩ = 3, etc. There are sixty-four combinations possible. The "d" denotes a lower delta. The plantar patterns are always read from left to right, and in making a formula for both feet the right is the numerator and the left the denominator of the fraction: $\frac{\text{W6d}}{\text{A27dd}}$.

In securing data on the probable occurrence of the various patterns and deltas, I took the prints of 191 newborn babies. The babies varied from one to seven days old and were taken in regular order as they were born at the Madison General Hospital. As some of the prints were impossible to read, due to errors in technic and otherwise, I secured only 163 double (both feet) prints; 342 single, of which 184 were male, 158 female, 172 right and 170 left. It is interesting to note that in a number of cases there was no trace of a pattern to be found, the whole field appearing only as a mass of dots. I feel that this is not due to an error in technic, but that the papillary ridges have not matured enough to produce definite lines. When this occurs it would be necessary to place the print in the undecipherable compartment.

Table I shows in detail the frequency of occurrence of the

different basic types of hallucal and plantar patterns, and of the various deltas. It is noticeable that the "A" and "W" patterns are the most frequent, while "C" occurs least often in the hallucal area. Only 19 whorls were found there which varied from the fundamental pattern.

TABLE I.—DETAILED TABLE SHOWING FREQUENCY OF OCCURRENCE OF VARIOUS PATTERNS AND DELTAS.

	Male.	Female.	Total.	Right.	Left.
Hallucal:					
A	87	79	166	87	79
B	22	19	41	23	18
C	3	3	6	4	2
O	5	8	13	6	7
W	58	39	97	47	50
tl	5	6	11	2	9
cp	2	0	2	0	2
lp	2	4	6	3	3
Delta:					
B	67	53	120	51	69
1	16	11	27	11	16
2	10	17	27	17	10
3	0	0	0	0	0
4	14	11	25	15	10
O	62	51	113	44	69
d	112	92	204	113	91
dd	10	15	25	15	10
ddd	0	0	0	0	0
Plantar:					
I O	150	123	273	133	140
U	11	10	21	13	8
∩	23	25	48	26	22
W	0	0	0	0	0
II O	68	59	127	55	72
U	111	94	205	112	93
∩	1	3	4	1	3
W	4	2	6	4	2
III O	162	143	305	150	155
U	19	14	33	20	13
∩	2	1	3	1	2
W	1	0	1	1	0

No lower deltas were found in 113 cases, 1 in 204, 2 in 25 and in no instances were all 3 found.

In the first plantar area no whorls were found and the open field was the most common. In the second area the "U" pattern predominated. In the third area the open field predominated again, and in only 1 case was a whorl found.

Of the digital deltas, 79 were found on 342 prints, and in no case was the third seen. The reason for this conspicuous absence of most of the deltas is that it is very difficult to make contact between the skin under the toes and the paper. Here again is another instance why the Cummins method cannot be used in this

work, because much of the description of the plantar areas depends upon these deltas.

The sex of the subject and whether the print was taken from the right or left foot seems to have very little influence upon the frequency of occurrence of the various patterns and deltas (see Table I).

Table II gives in detail the number of times the various types of patterns occurred, and it agrees in the main with that found by Wilder. "A" formulæ were found 168 times; "B," 41; "C," 6; "O," 13; "W," 114.

TABLE II.—TABLE SHOWING FREQUENCY OF OCCURRENCE OF THE SINGLE FORMULÆ.

A1	58	B3d	1	W6dd	4
A2	1	B5	2	W7d	6
A2d	3	B5d	14	W9	1
A3	1	B6d	1	W9d	1
A5d	61	B6dd	2	W13d	1
A6d	5	B7d	2	W15d	1
A6dd	7	B21dd	1	W17d	2
A7d	5	B33d	1	W21d	2
A9d	1	B37d	2	W21dd	5
A13d	1	B41d	1	W23dd	1
A17d	5	C1	1	W33	1
A20d	1	C5d	1	W33d	2
A21d	2	C6d	1	W37d	4
A21dd	5	C21dd	1	W45d	2
A23d	1	C37	2	W(tl)1	2
A29dd	1	O1	4	W(tl)5d	7
A33	1	O5	4	W(tl)7d	2
A33d	2	O5d	2	W(cp)5d	1
A33dd	1	O6d	2	W(cp)37d	1
A37d	5	O6dd	1	W(lp)5d	4
A41d	1	W1	21	W(lp)7d	1
B1	13	W2d	2	W(lp)37d	1
B3	1	W5d	39		

Next comes the problem of filing the prints. When they are taken it is advisable to give one set to the parents and to keep one for the hospital records in order that they may be used for comparison in the future, if necessary. For filing, it is suggested that a 5 by 8 inch card be used. At the top space is provided for recording the name and address of the parents, date, case number and the formulæ of the patterns. In the large space remaining the prints can be pasted (trimmed a bit if necessary). In this way not much space is used, and as both of the prints are pasted on a card there is less danger of one or both being lost. These cards are not to be placed with the baby's chart, but in a separate filing cabinet. The question of how many drawers it would be necessary to buy must be determined by the number of births occurring at the hospital. If there are only a few (150 to 200) a year, only a few drawers will be needed to start; but if there are several hundred during the year it would be advisable to purchase the whole twenty-five.

To come to the actual filing of the records. The hallucal patterns determine the drawer the card is to go into. The first drawer is labeled $\frac{A}{A}$, the second $\frac{A}{B}$ and so on. The complete list of combinations is:

$$\frac{A\ A\ A\ A\ A\ B\ B\ B\ B\ B\ C\ C\ C\ C\ C\ O\ O\ O\ O\ O\ W\ W\ W\ W\ W}{A\ B\ C\ O\ W\ A\ B\ C\ O\ W\ A\ B\ C\ O\ W\ A\ B\ C\ O\ W\ A\ B\ C\ O\ W}$$

Of course it is possible to put two or three of these primary classes into one drawer because patterns occur rarely in some of them (see Table III).

The secondary classification is found by referring to the number denoting the plantar patterns. There are 64 of these groups, and as there are two feet to be considered, right and left, it makes 4096 possibilities, or secondary subdivisions. These need to be made only from time to time, as new formulæ occur. The tertiary subdivision is determined by the lower deltas, and the order is:

$$\frac{o}{o}\ \frac{o}{d}\ \frac{o}{dd}\ \frac{o}{ddd}\ \frac{d}{o}\ \frac{d}{d}\ \frac{d}{dd}\ \frac{d}{ddd}, \text{ etc.}$$

Some of the compartments will soon be overcrowded, as $\frac{A1}{A1}$, and a simple method for further subdivision will have to be worked out. It has been suggested by Wilder that a ridge count be taken from the center of the hallucal pattern to delta B, but as delta B was found only 120 times in 288 cases, excluding B and O, it is impractical. It must be remembered that taking sole prints of a baby and of an adult are not the same thing by any means. The adult will hold his foot still, and will roll it to the medial side on request so that delta B will print, but a newborn baby will do no such thing, and if there is anything that can wiggle more than a little baby, I have yet to see it. This disinclination on the part of the baby to remain quiet is the chief reason why finger prints are not taken. As an aid to further subdivision of the more common patterns, I would suggest that the pattern on the ball of the great toe be incorporated in the general formula in some manner.

Let us suppose, for instance, that Mrs. A. says that the baby given her when she leaves the hospital is not her own, but another. How can we prove that it is her child? When the baby was born two sets of sole prints were made. One was given to the parents and one placed in the files. New prints are taken of the disputed child and compared with the two original sets, and if they are the same there can be no question as to its identity. But if they do not how can we determine who the child is? The formula of the disputed child is, let us say, $\frac{A1}{W5d}$. We would turn to that compart-

TABLE III.—SHOWING FREQUENCY OF OCCURRENCE OF COMPLETE FORMULÆ.

A1		A33		A13d		C5d		W2d	
——	17	——	1	——	1	——	1	——	1
A1		A3		W7d		B1		W21dd	
A1		A33d		A33d		C21dd		W5d	
——	2	——	1	——	1	——	1	——	3
A5d		A7d		W1		C6d		W1	
A2d		A37d		B1		C37		W5d	
——	1	——	2	——	1	——	1	——	14
A17d		A5d		A5d		O1		W5d	
A5d		A37d		B1		O5		W5d	
——	9	——	1	—	4	——	1	——	4
A1		A6dd		B1		A5d		W7d	
A5d		A37d		B5d		O1		W5d	
——	14	——	1	——	1	——	1	——	1
A5d		A21dd		B3		B5d		W13d	
A5d		A38dd		B5d		O1		W5d	
——	1	——	1	——	2	——	1	——	1
A7d		A7d		B5d		O6d		W15d	
A6d		A41d		B5d		O5d		W6dd	
——	1	——	1	——	2	——	1	——	1
A1		A6d		B7d		O6d		W5d	
A6d		A5d		B5d		W1		W6dd	
——	1	——	2	——	1	——	3	——	1
A21dd		B1		B21dd		A1		W21dd	
A6dd		A17d		B33d		W5d		W7d	
——	1	——	1	——	1	——	1	——	1
A7d		O5		B3d		A1		W5d	
A6dd		A37d		B37d		W5d		W21dd	
——	1	——	1	——	1	——	1	——	1
A27dd		O5d		B5d		A5d		W6dd	
A17d		A1		B37d		W6dd		W33d	
——	1	—	3	——	1	——	1	——	1
A2		W1		B6dd		A21dd		W9d	
A17d		A2d		B5		W21d		W37d	
——	1	——	1	—	1	——	1	——	1
A2d		W17d		O1		A7d		W1	
A20d		A5d		B6d		W33d		W37d	
——	1	——	3	——	1	——	1	——	1
A5d		W1		O5		A9		W21d	
A21d		A5d		B5d		W39d		W37d	
——	1	——	2	——	3	——	1	——	1
A5d		W5d		W5d		A1		W23dd	
A21dd		A5d		B5d		W1		W37d	
——	1	——	1	——	1	——	4	——	1
A6d		W37d		W7d		W1		W33	
A23d		A6d		B6d		W1		W45d	
——	1	——	2	——	1	——	1	——	1
A5d		W5d		W5d		W5d		W7d	
A29dd		A6dd		C37		W2d		W45d	
——	1	——	2	——	1	——	1	——	1
A1		W21dd		A6d		W17d		W9	
A33									
——	1								
A1									
A		B		C		O		W	
— 64		— 1		— 1		— 1		— 9	
A		A		A		A		A	
A		B		C		O		W	
— 2		— 13		— 1		— 1		— 41	
B		B		B		B		W	
A		B		C		O			
— 2		— 2		— 1		— 2			
O		O		C		O			
A		B		C					
— 16		— 5		— 1					
W		W		O					

ment in the file and by comparison the child could be identified. The number of different combinations possible with the simple method of formulation described above is more than one would expect at first glance. There are 25 hallucal combinations, 4096 plantar and 16 by the lower deltas. These figures multiplied together give 1,638,400 possibilities. Further subdivisions would give almost innumerable combinations.

The question of identity of a newborn baby rarely arises in a well-regulated hospital, but when it does it seriously affects all concerned. If a complete sole-print file has been carefully kept the matter can be settled easily in a very short time, and, perhaps, an expensive law suit averted.

It has been proved beyond all doubt that the papillary ridges on the balls of the fingers do not change their patterns throughout life, and it is only reasonable to suppose that those on the sole of the foot do not. However, it remains for some investigator to settle this point definitely.

Summary. 1. The new method of taking finger, palm and sole prints as devised by Prof. J. H. Mathews is far superior to the old ink method.

2. The method of formulation of the plantar patterns as worked out by Wilder is simple and practical.

3. The necessity of absolutely identifying the newborn babies is apparent to anyone giving a little thought to the matter, and is best done by sole prints.

4. Not only will prints prove valuable during the first few weeks of life, but in later years, when questions of identity often arise. It has been noticed many times that after death by fire or accident, when the body has been mutilated beyond recognition, that the soles of the feet remain intact, having been protected by the shoes. Identification would be a simple matter if sole prints of the individual were available. It would be a splendid thing for the country if it were required to file sole prints along with the birth certificate.

BIBLIOGRAPHY.

1. Hepburn, David: The Intertegumentary Grooves on the Palm of the Hand and the Sole of the Foot of Man and the Anthropoid Apes, Jour. Anat. and Physiol., 1893, **27**, 112.

2. Hepburn, David: The Papillary Grooves on the Hands and Feet of Monkeys and Man, Sci. Trans. Royal Dublin Soc., 1893, **5**, 525.

3. Kidd, W.: On Imbrication of the Papillary Ridges in Man, Jour. Anat. and Physiol., 1903, **39**, 413.

4. Kidd, W.: The Papillary Ridges and the Papillary Layer of the Corium in the Mammalian Hand and Foot, Jour. Anat. and Physiol., 1907, **41**, 35.

5. Wilder, H. H.: Palms and Soles: Am. Jour. Anat., 1902, **1**, 423.

6. Wilder, H. H.: Palm and Sole Impressions and their Uses for Purposes of Personal Identification, Popular Sci. Monthly, September, 1903, p. 385.

7. Wilder, H. H.: Palm and Sole Studies, Biol. Bull., 1916, **30**, 125 and 211.

8. Cummins, H., and Sicomo, J.: Plantar Epidermal Configurations in Low-grade Syndactylism of the Second and Third Toes, Anat. Rec., 1923, **25**, 355.

9. Kidd, W.: The Arrangement of the Papillary Ridges on the Human Hand and Foot, Jour. Anat. and Physiol., 1909, **43**, 291.

10. Wilder, H. H., and Wentworth, Bert: Personal Identification, 1918, Badger.

THE INFLUENCE OF THE GALL BLADDER ON INTESTINAL MOTILITY.

By Benjamin M. Bernstein M.D.,
BROOKLYN, N. Y.

(Preliminary report read before Gesellschaft für Innere Medizin of Vienna, November 6, 1924.)

The question of gall-bladder function as well the diagnosis and treatment of its diseased conditions have held a prominent part on the stage of medical research in the last few years. Despite considerable work we are still in the dark on many fundamental facts concerning this interesting organ. We have been taught that its function is that of a reservoir and medium for concentrating the bile during its stay there. The gall-bladder bile is darker and of greater consistency than the liver bile; it has a greater percentage of bile salts and cholesterin; it contains mucin, a nucleo-albumin, not found in the liver bile. If the gall bladder is purely a reservoir, why was it placed on a side path, instead of in a direct line as in the kidney-ureter-bladder-urethra system? Furthermore, why is a reservoir supplied with glands and deep ducts lined with glandular epithelium, if the latter have no secreting function? the mucous membranes, which secrete mucus only, have no glands. These and other questions in gall-bladder function still await solution at the hands of modern scientific research.

In the field of diagnosis, both the roentgenologist and the internist have tried their skill with but questionable success. George, L. G. Cole, Leonard, and others, have written much on the "direct" and "indirect" evidence of gall-bladder disease on the roentgen-ray film. The percentage of cases in which positive roentgen-ray shadows of the gall bladder and its contents can be shown and the diagnostic value of such visualization, are questions of doubtful significance. As a matter of fact, both L. G. Cole and Leonard have agreed that the "indirect" signs are of much greater value than the "direct" method (by indirect signs, we refer to the changes produced by the gall-bladder disease on surrounding organs).

Latterly, Graham, W. H. Cole, and Copher of St. Louis, have brought out another method, that of visualizing the gall bladder and its contents by filling it with an opaque contrast solution. For this purpose they have used the calcium salt of tetrabromphenolphthalein which is excreted by way of the bile and thus finds its way into the gall bladder after intravenous injection. The method is not without discomfort and even danger to the patient, is difficult of operation, and extremely problematical in its diagnostic value.

When one studies the autopsy records of the large medical centers in this and other lands, he finds that the occurrence of gall stones

in man is a rather frequent one. Statistics seem to show that 10 to 12 per cent of all people coming to autopsy have gall-bladder calculi, with and without symptoms. Such being the case, one doubts the diagnostic value of mere visualization of the gall bladder and its contents, regardless of how perfect in this respect any method may become. One is inclined to divide his cases into "calculus carriers" and "calculus patients."

The secondary effects of gall-bladder affection, however, do offer valuable data by which our diagnostic ability may be bettered. It also gives us clues, which if properly studied and evaluated, will help us to clear up some of the questions regarding gall-bladder function. It is a well-known fact that gall-bladder disease is the most frequent cause for the production of reflex gastrointestinal symptoms. During the course of routine roentgen-ray examination of patients with gastrointestinal symptoms, we always made a six-hour observation after the ingestion of a barium and buttermilk mixture. We found a number of cases with an unusual type of intestinal motility, and learned that these patients had been referred to us as cases of cholecystitis or cholelithiasis; some of these were operated upon subsequently and pathological states of the gall bladder were found.

To describe intestinal motility of the barium meal, we must divide the opaque column as having a "head, a body and a tail." Depending on where the various parts of the column are found at the six-hour period, we classify the type of motility as normal, hypermotility and hypomotility. In these cases we observed a type heretofore undescribed, which we have chosen to call "strung-out," in other words, we found that although the "head" of the column was seen in the distal half of the colon, the "tail" was still in the jejunum with the "body" "strung-out" between the two points. Barring diffuse peritonitis with extensive adhesions, this type of motility was never observed in any other gastrointestinal disease or affection. Of course we did see a number of cases of gall-bladder disease without this "strung-out" motility; but whenever we saw this disturbance, we found we were dealing with a gall-bladder affection.

Through the kindness of Professor Wenckebach and the coöperation of his roentgenologist, Dr. Hitzenberger, the writer was enabled to perform a series of experiments on dogs in an attempt to discover the cause of this rather peculiar phenomenon. The dogs were fed with a meal consisting of barium and yoghurt, in addition to the various other substances used in our investigations, observations being made six hours after the ingestion of the meal. We first determined the normal intestinal motility of 5 dogs on repeated examination. Then 4 of the dogs were operated upon and complete cholecystectomy performed; the skin was permitted to heal before observations were again made. When these animals were then examined, we found that each one of the 4, now showed a "strung-out"

motility on repeated search. It was natural to assume that here was the cause of our unusual motility disturbance; that it was the absence of the gall-bladder function which was the factor, whatever that function may acutally prove to be. Drawing conclusions a bit further, we were able to say that whenever we saw this motility irregularity in a patient with gastrointestinal symptoms, we were dealing with an absence of gall-bladder function, due to closure of the cystic duct, regardless of what the cause of such closure may be; and that those cases of gall-bladder disease which did not show this change, had no obstruction of the cystic duct.

How were we to explain our observations in the light of our present knowledge? We found an observation by Rohde that 72 per cent of patients who had cystic duct closure, showed a hypoacidity, which persisted in 90 per cent of them, years after cholecystectomy had been performed. Hohlweg believes the achylia found by him in cases of cystic duct closure, to be due to the absence of gall-bladder function, be that what it may. The following experiments were then performed in order to discover, if possible, what there might be in the gall-bladder bile which made it different from the liver bile, the absence of which substance created this disturbance in intestinal motility.

Experimental Work. EXPERIMENT 1. The 4 cholecystectomized dogs and 1 normal dog were given 5 cc each, of gall-bladder bile with their barium meal. After six hours, we found that the animals operated upon had their motility restored to normal, and that the normal dog showed an increase in his usual motility. It is rather interesting to note at this point, that Dastre in 1891 observed that feeding dogs with gall-bladder bile produced in them a diarrhea.

EXPERIMENT 2. Sodium taurocholate and glycocholate (0.4 gm. each) were added to the meals of the 5 dogs. There was no change in motility, either in the normal or in the cholecystectomized animals.

EXPERIMENT 3. An alcoholic extract of gall-bladder mucosa was made and given to the dogs with their meals, without change in motility.

EXPERIMENT 4. The dogs were fed with an aqueous extract of gall-bladder mucosa added to their meals, without influencing the motility either in the normal or in the operated animals.

EXPERIMENT 5. Two ether extracts were prepared: One, after an aqueous and an alcoholic extract had been taken from the mucosa; another, from the fresh gall-bladder mucosa. Both of these extracts, when given to the dogs with the barium meal, showed a restoration to normal motility in the operated dogs and an increase in motility in the normal dog.

EXPERIMENT 6. Cholesterin (0.3 gm.) with the meal showed a restoration to normal motility in the cholecystectomized dogs, and no effect in the normal dog.

EXPERIMENT 7. Cholesterin (0.3 gm.) plus ether extract of mucosa added to the meal produced no change in the dogs operated upon, and showed some increase in motility in the normal.

Each one of the above experiments was performed at least twice and therefore the element of chance can be definitely ruled out.

Now let us make a resume of our observations before we draw conclusions. We find that the feeding of gall-bladder bile produces a restoration of the disturbed motility to normal, in the cholecystectomized animals, and an increase in motility in a normal dog. Furthermore, the bile salts given in fairly large doses are ineffective; the same applies to the aqueous and alcoholic extracts of gall-bladder mucosa. Cholesterin produces a restoration to normal motility in the operated dogs, and has no effect on the motility of the normal animal. Finally, an ether extract of gall-bladder mucosa restores the disturbed motility in the cholecystectomized dogs and an increase of motility in the normal dog; also, whereas cholesterin alone does restore the motility in the experimental dogs and has no effect in the normal, when given with the ether extract of gall-bladder mucosa, it produces then no effect in the cholecystectomized dogs, though the combination does increase the motility of the normal animal.

What are the conclusions which can be drawn from these interesting observations? First, that the gall bladder is not merely an organ of concentration and a reservoir for the excess bile. After its removal, there is a definite disturbance in intestinal motility. Further, the feeding of whole gall-bladder bile, causes a restoration of the disturbed motility to normal. Then again, large doses of bile salts which may be concentrated in the bladder produce no change in the irregular motility. Finally, cholesterin, a substance likewise concentrated in the bladder, does affect the disturbed motility in the cholecystectomized animals, though it has no effect in the normal dog; however it loses its efficacy as such when combined with an ether extract of gall-bladder mucosa, given to the dogs without their gall bladders.

Second, the gall bladder has a definite secretion, the product of its glandular activity, which has a stimulative, perhaps a regulatory influence on intestinal motility. An ether extract of gall-bladder mucosa, prepared even after an aqueous and an alcoholic extract has been taken, produces a definite restoration of the disturbed motility caused by cholecystectomy. Moreover this extract seems to have an inhibitory effect on the apparent stimulative effect of cholesterin in intestinal motility in the cholecystectomized animals. Furthermore, whereas cholesterin had no effect in the normal dog that had his gall-bladder function intact, this ether extract did affect the motility when given with the cholesterin, demonstrating its strength even in the normal.

Conclusions. We believe that: (1) This substance secreted from the gall bladder is of hormonal type, an activator; (2) that it has a regulatory effect on intestinal motility, and (3) that its absence produces an imbalance in the normal correlated action of the circular and longitudinal muscle fibers of the intestinal tract.

We venture to suggest, merely as a theoretic possibility, that the permanent or even temporary absence of this substance in the gall bladder, may be the exciting cause for the production of the primary cholesterin calculus, in permitting a precipitation of the cholesterin in the bile, where it may be held in solution by the presence of this substance.

REFERENCES.

Bernstein, B. M.: Wien. med. Wchnschr., 1924, **50**, 2683.
Graham, E. A., and Cole, W. H.: Jour. Am. Med. Assn., 1924, **82**, 613.
Graham, E. A., Cole, W. H., and Copher, G. H.: Ann. Surg., 1924, **80**, 473.
Carman and Counseller: Am. Jour. Roentgenol., 1924, **12**, 403.
Cole, L. G., and George: Boston Med. and Surg. Jour., 1915, **172**, 326.
George, A. W., and Leonard, R. D.: Am. Jour. Roentgenol., 1917, **4**, 321.
Pfahler: Jour. Am. Med. Assn., 1914, **62**, **17**, 1304.
Leonard, R. D.: Am. Jour. Roentgenol., 1923, **10**, 521.
A. Dastre: Archives de Physiologie, 1890, No. 2, 318.
Rohde, C.: Muench. med. Wchnschr., 1920, **67**, 150.
Hohlweg: Deutsch. Arch. f. klin. Med., 1912, **108**, 255.
Sweet, J. E.: International Clinics, 1924, **34** s., 1, 187.

EXPERIMENTAL STUDIES ON THE COLOR OF THE BILE FROM THE GALL BLADDER AND LIVER.

By A. Winkelstein, M.D.,

AND

P. W. Aschner, M.D., F.A.C.S.,

NEW YORK.

(From the Surgical Laboratories of the College of Physicians and Surgeons, Columbia University, New York.)

The introduction and wide clinical application of the Meltzer-Lyon method of studying the biliary tract has given rise to controversy concerning important points in the physiology of the gall bladder. Experimental studies upon the pressure factors in the duct system of the dog[1] and upon the entrance of bile into the duodenum[2] have been reported by us. These studies were undertaken in an effort to clarify the mechanism of the entrance into and the exit of bile from the gall bladder.

The origin and significance of the dark "B" bile is of prime importance in the application of the Meltzer-Lyon test. Lyon

and those who follow his teachings maintain that dark bile comes from the gall bladder. Others, notably Einhorn,[3] maintain that this is not invariably the case, and that dark bile may be recovered in patients who have had a cholecystectomy performed. We have attempted, therefore, to study this question experimentally in the dog by intubating separately the common duct, one hepatic duct and the duodenum, with the gall bladder *in situ*, and with the gall bladder excised.

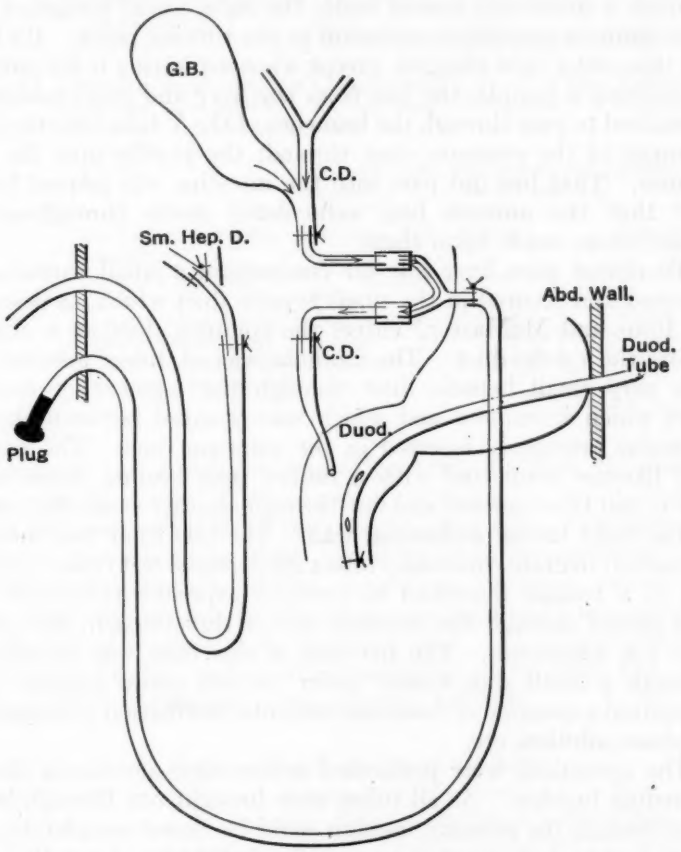


FIG. 1.—Diagram: G. B., gall bladder; Duod., duodenum; C. D., common duct; Sm. Hep. D., small hepatic duct.

Method of Study. We are indebted to Drs. Rous and McMaster,[4] of the Rockefeller Institute for their method of avoiding infection by the use of long intra-abdominal rubber tubes.

By using a system of cannulas and connecting tubes, bile was permitted to enter the duodenum in a relatively normal manner, but could be sampled at will from the ducts and the duodenum (Fig. 1). A small glass cannula was introduced into the common

duct toward the liver and tied in securely at a point below the entrance of the cystic duct. A second cannula was introduced into the common duct toward the papilla of Vater at a point lower down, and similarly secured. The duct was completely severed between them. By short pieces of tubing the cannulas were connected with the branches of a small glass Y tube, and the latter secured by a suture through the round ligament. From its long arm a tube was led down into the pelvis and then upward and out through a small stab wound under the right costal margin, a bent glass cannula preventing occlusion at the turning point. By keeping this outlet tube plugged, except when aspirating it for purposes of securing a sample, the bile from the liver and gall bladder was permitted to pass through the branches of the Y tube into the lower segment of the common duct through the papilla into the duodenum. That bile did pass into the intestine was proved by the fact that the animals had well-colored stools throughout the observations made upon them.

To obtain pure liver bile for comparison a small cannula was inserted and secured in the small hepatic duct which, as described by Rous and McMaster,[5] enters the common duct at a distance below the cystic duct. The cannula was at times inserted into this very small hepatic duct through the segment of common duct which it entered and which was situated between the two cannulas previously inserted in the common duct. The cannula was likewise connected with a rubber tube leading down to the pelvis and then upward and out through another small stab wound in the right lateral abdominal wall. The bile from this tube was permitted to drain constantly into a small sterile test tube. According to a technic described in previous experiments,[6] a soft tube was passed through the anterior wall of the stomach, and guided into the duodenum. The free end of this tube was brought out through a small stab wound under the left costal margin. This permitted aspiration of duodenal contents, instillation of magnesium sulphate solution, etc.

The operations were performed under ether anesthesia through a median incision. As all tubes were brought out through lateral stab-wounds the primary incision could be closed completely. The procedure took from one to one and a half hours, depending upon the technical difficulties of introducing the cannulas into the ducts, and securing them in proper position.

Experiments. EXPERIMENT 1.—Dog No. 3920. Male, weighing 12 kilos. Ether anesthesia. Median laparotomy. The procedures above detailed were carried out. The observations are recorded in Table I. The animal died on the fifth day of general peritonitis, due to rupture of a small abscess around the gastric fistula. The tubes and cannulas were found in good order.

TABLE I.—GALL BLADDER IN SITU.

Time, postoperative.	Conditions.	Color and Character of the Bile or Fluid.		
		Common Duct aspiration.	Hepatic Duct drainage.	Duodenum aspiration.
20 hours	Fasting	5 cc; dark green-brown	3 cc; light brown	7 cc; lighter brown.
21 "	Fasting; 40 cc $MgSO_4$ in duodenum	8 cc; similar, dark	1½ cc; light yellow	Yellow.
25 "	Fasting	2½ cc; dark, tarry	Light brown	Light brown.
44 "	Fasting (drank water)	8 cc; dark, tarry	4 cc; yellow bile	Yellow.
45 "	Fasting; 40 cc $MgSO_4$ (as above); observation for 1 hour	3 cc; very dark brown	1 cc; yellow	Pale yellow.
3 days	Fasting	3 cc; very dark brown	9 cc; yellow (collected over 24 hours)	Yellow.
3 "	Fasting; 40 cc $MgSO_4$ (as above)	2 cc; very dark brown	Yellow	Yellow.
3 "	Ate sugar and eggs	4 cc; very dark brown	Yellow	Yellow.
4 "	4 hours after eating broth, bread, meat	5 cc; greenish-brown	Yellow	Yellow.
4 "	5 hours after food, 40 cc $MgSO_4$ (as above)	Yellow-brown	Yellow	Yellow

Comment. Although this animal lived only five days, the observations seem of value. With the single exception of an observation made five hours after food, the common duct tube contained dark, tarry or greenish-brown, bile (mixed gall bladder and liver bile). The duodenal contents at the same time, however, varied from light yellow to medium brown, hence not accurately mirroring the appearance of the bile in the common duct. The isolated hepatic duct drained a light yellow bile throughout, either after fast, after food, or after instillation of magnesium sulphate.

TABLE II.—GALL BLADDER IN SITU.

Time, postoperative.	Conditions.	Color and Character of the Bile or Fluid.		
		Common Duct aspiration.	Hepatic Duct drainage.	Duodenum aspiration.
15 minutes	Under anesthesia	Dark, green-brown	Light yellow-brown	Brown.
19 hours	Fasting	3 cc; dark green-brown	1 cc; lemon-yellow	Turbid brown.
24 "	Drank water only; 40 cc $MgSO_4$ injected in duodenum	2 cc; dark green-brown	½ cc; lemon-yellow	Watery brown.
48 "	Dog died; cause of death not found at the autopsy.			

EXPERIMENT 2.—Dog. No. 3923. Male, weighing 13 kilos. The procedure was the same as in the previous experiment. This animal died forty-eight hours after operation, and although the observations are therefore of limited value they are recorded in Table II. The cause of death was not ascertained at autopsy.

EXPERIMENT 3.—Dog No. 3924. Female, weighing 12 kilos. In this animal the upper cannula was inserted into the common duct at a point below the entrance of the posterior hepatic duct. All the bile was therefore sidetracked through the Y tube (Fig. 2).

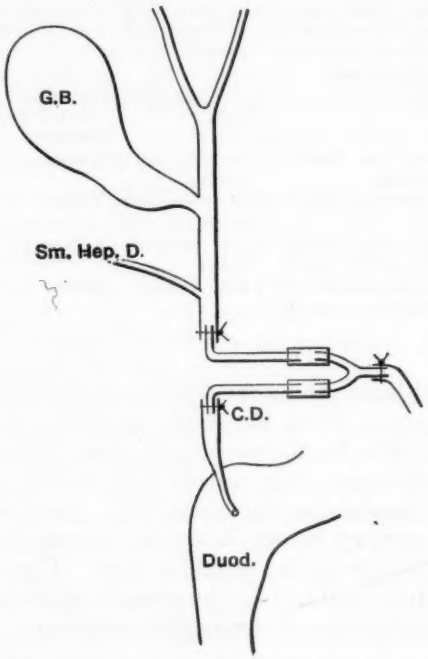


FIG. 2.—Diagram: Common duct shunted below entrance of the small hepatic duct.

Cholecystectomy was performed. The duodenal tube was inserted as in the preceding experiments. At autopsy, on the thirteenth day, the tubes were well walled off by adhesions. The ducts were not dilated. The cystic stump showed no evidence of regeneration.

Comment. In this experiment, in which cholecystectomy was performed, the bile in the common duct and the duodenum was observed during the fasting state, after food and after the injection of magnesium and sodium sulphate into the duodenum. Throughout the entire experiment, after the first twenty-four hours, the bile in the common duct, although varying in the rate of flow, was constantly a light yellow color and quite thin. Even after a

prolonged fast of forty-eight hours, and after a markedly increased flow following the eating of meat, the color did not become darker. It was also noticed that the duodenal contents did not correspond very closely to the common duct contents, varying from a pale opalescent to a lemon-yellow to a muddy brown fluid.

TABLE III.—GALL BLADDER EXCISED.

Time, postoperative.	Conditions.	Color and Character of the Bile or Fluid.	
		Common Duct aspiration.	Duodenum aspiration.
24 hours . .	Fasting	1½ cc; dark green-brown	Lighter brown.
25 " . .	Fasting; 40 cc $MgSO_4$ in duodenum	1½ cc; dark green-brown	Brown.
32 " . .	15 hours after, meat and water	2 cc; yellow-brown	Lighter brown.
33 " . .	15 hours after, meat and water; 40 cc $MgSO_4$ in duodenum	½ cc; lighter yellow-brown	Yellow fluid.
3 days . .	15 minutes after meat, bread and broth	3 cc; golden-yellow	3 cc; lighter yellow.
4 " . .	Fasting 24 hours	3 cc; golden-yellow	Lighter yellow.
4 " . .	Fasting 24 hours; 40 cc $MgSO_4$	2½ cc; lighter yellow	Yellow-tinged.
4 " . .	15 minutes after, food	3 cc; golden-yellow	Turbid, faint yellow.
5 " . .	Fasting 26 hours	2 cc; golden-yellow	Dirty brown.
5 " . .	Fasting 26 hours; 40 cc $MgSO_4$	½ cc; golden-yellow	Lemon-yellow.
5 " . .	Eating 100 gm. meat	In 10 minutes, 5 cc; golden-yellow	Lemon-yellow.
6 " . .	Fasting 24 hours	1½ cc; golden-yellow	Lemon-yellow.
7 " . .	Fasting 18 hours	2 cc; golden-yellow	Lemon-yellow.
7 " . .	Fasting 18 hours; 25 cc Na_2SO_4	1 cc; lighter golden	Lemon-yellow.
7 " . .	Bread and water	2½ cc; lighter yellow	Lemon-yellow.
8 " . .	Fasting 24 hours	2 cc; golden-yellow	Muddy brown.
8 " . .	Fasting 24 hours; 40 cc $MgSO_4$	1 cc; golden-yellow	Lemon-yellow.
8 " . .	Ate 100 gm. meat	In 3 minutes 5 cc; golden-yellow	Lemon-yellow.
9 " . .	Fasting 24 hours	2½ cc; golden-yellow	Lemon-yellow.
9 " . .	Fasting 24 hours; 40 cc $MgSO_4$	In 20 minutes 2½ cc; golden-yellow	Pale fluid.
9 " . .	Ate 150 cc meat and broth	In 20 minutes 5 cc; golden-yellow	Pale fluid.
11 " . .	Fasting 48 hours	3½ cc; golden-yellow	Pale yellow.
12 " . .	Fasting 18 hours	2½ cc golden-yellow	Pale yellow.

EXPERIMENT 4.—Dog. No. 3928. Male, weighing 10 kilos. Two cannulas were placed in the common duct and connected up as in the preceding experiment. The duodenum was not intubated at this time. Aspiration of the tube fifteen minutes after the operation revealed the presence of dark green-brown bile in the common duct. During the next eight days the bile was aspirated daily

fifteen to eighteen hours after food, and on each occasion 8 to 12 cc of dark green-brown to tarry, viscid bile was obtained. On the eighth day, under ether anesthesia, the abdomen was opened and a cholecystectomy was performed. The gall bladder was normal, and contained 5 cc of dark bile. The ducts were not dilated. The dog recovered perfectly from the operation, and observations were made on the appearance of the bile in the common duct for nine weeks. These are given in Table IV.

TABLE IV.—AFTER CHOLECYSTECTOMY.

Time after Cholecystectomy.	Conditions.	Character of the Bile. Common Duct aspiration.
24 hours	Fasting 60 hours	3 cc; medium brown.
2 days	4 hours after food	3½ cc; golden-yellow.
3 "	Fasting 24 hours	3 cc; golden-yellow.
3 "	Immediately after food	1½ cc; golden-yellow.
4 "	Immediately after food	2½ cc; golden-yellow.
7 "	Fasting 60 hours	2½ cc; slightly darker.
7 "	Immediately after eating meat	1 cc; golden-yellow.
8 "	Fasting 24 hours	2½ cc; golden-yellow.
9th to 16th day	Fasting 24 hours	2½ cc; golden-yellow (each day).
9th to 16th day	Immediately after food	1½ cc; golden-yellow (each day).
17th to 20th day	Fasting 72 hours	2 cc; medium brown bile.
During the next 26 days	Fasting 18 to 24 hours	2½ cc; golden-yellow (each day).
During the same 26 days	Immediately after food	2 cc; golden-yellow (each day).

Nine weeks after the cholecystectomy, under ether anesthesia, a duodenal fistula was made opposite the papilla of Vater and a soft tube sewed in it at this site.

Observations. Twenty-four hours postoperative: Dog fasting; 2½ cc of yellow bile in the common duct, and the duodenal contents were light yellow; 40 cc of 25 per cent magnesium sulphate solution was injected through the fistula into the duodenum. During the next hour there was no change in the color of the bile in the common duct or in the duodenum. Forty-eight hours postoperative: Fifteen hours after food similar observations were made. Seventy-two hours postoperative: Dog fasting twenty-four hours; both in the fasting animal and after magnesium sulphate the bile still remained unchanged in color. Four days after operation the dog died.

Autopsy. The cause of death was not found. The common duct above the upper cannula was widely dilated, measuring 2 cm. in width and 3 cm. in length, and contained light yellow bile. The short portion of the common duct below the second cannula

was also somewhat dilated. The liver tissue appeared normal with no widening of the intrahepatic ducts. Extrahepatic dilatation of the biliary duct system follows cholecystectomy almost regularly in experimental animals.[7]

Comment. This experiment provided the exceptional opportunity for studying the bile from the common duct with the gall bladder in, and after its removal, and later when influenced through a duodenal fistula. It is apparent that in a fasting animal with its gall bladder *in situ* the bile in the common duct varies from a dark greenish-brown to a brown-black in color and is quite viscid. After cholecystectomy in the same animal, however, with the exception of the first twenty-four hours after the operation and after a three-day fast at which times it may be medium brown. the bile is invariably and uniformly lemon to golden-yellow in color and is quite thin. The injection of magnesium sulphate in the duodenum of the cholecystectomized dog did not change the color of the bile in the common duct.

Discussion. The experimental results indicate that the gall bladder is the source and cause of the dark bile. Apparently the bile coming directly from the liver, although containing a varying amount of bilirubin, is always yellow. The bile, however, from the gall bladder and liver (in the common duct) of the fasting animal is quite dark, ranging from a tarry or deep greenish-brown to a dark brown. That the gall bladder is responsible for this change in appearance is proved by the fact that after cholecystectomy the same animal, fasting, feeding or influenced by magnesium sulphate in the duodenum, exhibits only yellow bile in the common duct.

To what extent these experiments are applicable to clinical physiology, especially the Meltzer-Lyon test, may not be conclusively stated from our experiments. In the Meltzer-Lyon test the sequence of bile colors is observed in the duodenal contents, while in these experiments the observations are concerned chiefly with the types of bile found in the biliary ducts. It may be said, with reference to our observations of the duodenal contents, that their color imitates somewhat but not closely, the appearance of the bile in the common duct. Probably local dilution and chemical factors change the appearance of the duct bile.* Nevertheless, it seems highly probable that the dark color of the duodenal specimen which is obtained clinically in the normal individual by the Meltzer-Lyon method is caused by the gall bladder. Inasmuch as our experiments deal only with normal animals, nothing can be said of the appearance of the bile in certain pathological states, either local or general, which may modify the color of the bile.

Summary. By means of cannulas placed in the biliary ducts and connected as described above, it was possible to observe the appear-

* In a number of these and previous experiments the intestine of dogs in which the indwelling duodenal tube was carried for a number of days showed erosions of the mucous membrane in the vicinity of the end of the tube.

ance of bile from the dog's liver alone (through one hepatic duct) and from the gall bladder and liver together (through the common duct). By means of a gastroduodenal tube, the contents of the duodenum could likewise be observed. These fluids could be sampled separately and simultaneously without diverting the bile from the intestinal tract to any great extent. The observations were made in animals with the gall bladder *in situ* and after its excision. With the exception of a possible change in the rate of filling and emptying of the gall bladder, due to the artificial elongation of the common duct system, relatively normal conditions were maintained.

1. Bile in the common duct of fasting dogs under the experimental conditions was dark greenish-brown in color and almost tarry in consistency, when the gall bladder was *in situ*.

2. Bile obtained directly from the liver, that is, from a hepatic duct, was a light yellow color whether the dog was feeding or fasting. Exceptionally it was of a medium brown color in the first twenty-four hours after operation.

3. After cholecystectomy the bile from the common duct was light yellow and thin in consistency whether the dog was feeding or fasting.

4. The instillation of 25 per cent magnesium sulphate solution into the duodenum was not followed by any change in the color of the bile from the common duct either before or after cholecystectomy, under these experimental conditions.

REFERENCES.

1. Winkelstein and Aschner: Am. Jour. Med. Sci., 1924, **168**, 812.
2. Winkelstein and Aschner: Am. Jour. Med. Sci., 1925, **169**, 679.
3. Einhorn: New York Med. Jour., 1921, **113**, 313; 1921, **114**, 262; 1922, **116**, 188.
4. Rous and McMaster: Jour. Exper. Med., 1923, **37**, 11.
5. Rous and McMaster: Jour. Exper. Med., 1921, **33**, 731; 1921, **34**, 47 and 75.
6. Winkelstein and Aschner: Am. Jour. Med. Sci., 1924, **168**, 749.
7. Judd and Mann: Surg., Gynec. and Obst., 1917, **24**, 437.

AN ESTIMATION OF THE CLINICAL VALUE OF THE VAN DEN BERGH TEST.*

By Elizabeth Glenn Ravdin, M.D.,

HENRIETTA HECKSHER MEMORIAL FELLOW, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

(From the William Pepper Laboratory of Clinical Medicine and the Medical Division of the University of Pennsylvania.)

The work discussed in this paper is the result of the application of the van den Bergh test for bilirubin in the blood serum in 140

* Read before the Pathological Society of Philadelphia.

cases in which there appeared to be an indication for such a test. It was undertaken with a view to determining the clinical accuracy and value of the test.

The methods previously in use for determining the presence of bile pigment in the serum were of two types—one depending upon the oxidation of bilirubin to biliverdin and the other upon the comparison of the color of the serum with a standard which approximated the color of normal serum. The first type of test, of which the Gmelin test is an example, depends upon the development of the green color of oxidized bilirubin when concentrated nitric acid is added to the serum. A concentration of bilirubin high enough to give a positive reaction is also high enough to produce discoloration of the tissues; so as a method of determining small amounts of bilirubin in the serum this group of tests is of no value. In the second type, as in the Meulengracht[1] test, the color of the serum is compared to a standard color, a dilute solution of potassium bichromate for example, which is so prepared that it matches the color of the average normal serum. The serum must then be diluted to match the standard, the amount of dilution being measured. The possiblities of error in this method are several. In the first place the test is not specific for bilirubin. Though they occur but rarely, other pigments may discolor the serum, such as carotin, biliverdin and perhaps urobilin. Also, slight hemolysis, which not uncommonly occurs after the blood is collected, will make it impossible to compare the serum with the standard. The most important source of error is due to the wide variation in the color of normal sera, so that slight variations due to increased bilirubin content will fall within the necessarily wide limits of the normal readings.

Van den Bergh,[2] in his search for a method by which small variations in the bilirubin content of the serum could be detected, recalled the diazo reaction which Ehrlich[3] had described in 1883. The reaction depends upon the development of an azo dye, azobilirubin, when an acid solution of a diazonium salt is added to an alcoholic solution of bilirubin. Pröscher,[4] in 1900, identified and isolated this dye, but no clinical use of the reaction was made until the work of van den Bergh and Schnapper[5] in 1913. These latter experimenters found that pure bilirubin in a dilution of 0.7 mg. per liter gave a positive reaction to this test, and that biliverdin and other substances in the blood serum did not react to it. This then opened the way for the study of inaugural stages in diseases in which variations in the concentration of bile pigment in the blood occur.

While using the diazo reaction for quantitative determinations of the bilirubin in serum, van den Bergh noticed that in certain cases of jaundice it was unnecessary to bring the bilirubin into an alcoholic solution to obtain the azo dye, but that merely the addi-

tion of the diazo reagent produced the reaction. It was evident that bilirubin might be present in the serum in different forms. He then found that in the cases in which a tumor or stone caused obstruction of the common duct the addition of alcohol was unnecessary, and that this was also true of normal diluted bile. In the cases in which bilirubinemia was associated with a blood disease the addition of alcohol was necessary to produce an immediate reaction. Also in hemorrhagic effusions into serous cavities when the presence of bilirubin was determined quantitatively an alcoholic solution was necessary to produce the prompt diazo reaction. From these observations he drew conclusions which led to a new conception of jaundice. While it is true that this conception is based almost entirely on theory, it is at present the best interpretation of the different reactions obtained in the various types of jaundice.

The two types of jaundice which van den Bergh differentiated between are to be understood as two general groups, depending upon the location and type of the pathological lesion. For an understanding of this classification a brief summary of the theories of pigment formation must be given.

The reticuloendothelial cells, found most abundantly in the liver, but also in the spleen and lymph glands as well as in other portions of the body, are, according to the work of Kupffer,[6] Aschoff,[7] McNee[8] and others, concerned with the breaking-down of the erythrocytes and the formation of bilirubin from the liberated hemoglobin. The bilirubin which is thus formed is then presumably present in some form in the blood stream. From the blood it is absorbed by, or passes through, the polygonal cells which line the biliary capillaries and is excreted by way of the bile. The bilirubin found in small amounts in the serum of normal persons and in greater amounts, due to increased hemolysis, in such conditions as ictero-anemia reacts differently from the bilirubin in an obstructive jaundice. The latter, as stated previously, reacts in the same manner as the bilirubin found in the bile. To the jaundice of obstruction van den Bergh gave the name "mechanical jaundice," while the jaundice of hemolysis or of liver disease he calls "dynamic jaundice". He assumes that the reason for the difference in reaction of the two is due to some action which the polygonal cells may have on the bilirubin, and therefore any pigment which has passed through these cells is of the obstructive type.

Method. Five cubic centimeters of blood is drawn from the vein into a dry test tube and allowed to clot. The serum is then removed by a pipette.

The Qualitative Test or Direct Reaction. To 1 cc of serum is added 1 cc of freshly prepared Ehrlich's diazo reagent. The time of the appearance of the maximum color is noted. If a reddish-

violet color develops within the first thirty seconds the direct reaction is said to be immediate. If no color appears until after thirty seconds, but does appear later, and it may not appear for as long as an hour, the reaction is delayed direct. If no color appears it is a negative reaction. If some color appears before thirty seconds, but grows more intense after that time, it is a mixed reaction, immediate and delayed, or biphasic direct.

The diazo reagent, which must be made immediately before the test is made, is a mixture of two solutions, each of which will keep for a month at least.

Solution A.

Sulphanilic acid	1 gm.
Concentrated HCl	15 cc
Distilled water	q. s. 1000 "

Solution B.

Sodium nitrite	0.5 gm.
Distilled water	100 cc.

To 25 cc of Solution A add 0.75 cc of Solution B.

The Quantitative Test or Indirect Reaction. To 1 cc of serum add 2 cc of 96 per cent ethyl alcohol and centrifuge. To 1 cc of the supernatant fluid add 0.25 cc of Ehrlich's diazo reagent and 0.5 cc of 96 per cent ethyl alcohol.

The result will vary from a faint pink color, as in normal serum, to a deep violet, depending on the amount of bilirubin present. The color is read in a colorimeter, such as the Hellige, against a standard, made up as follows:

STANDARD.

Solution I.

Ammonium ferric alum	0.1508 gm.
Concentrated HCl	50 cc.
Water	q. s. 100 "

This is a stable solution, keeping indefinitely. It is 1 to 320 normal.

Solution II.

Solution I	10 cc.
Concentrated HCl	25 "
Water	q. s. 250 "

This solution will keep one month. It is 1 to 8000 normal. The standard is made up of:

Solution II	3 cc.
10 per cent ammonium sulphocyanate (or 20 per cent potassium sulphocyanate)	3 "
Ether	12 "

Shake thoroughly.

The ether extracts the color from the solution and forms a supernatant layer which is transferred to the colorimeter as the known

standard. In cases in which the concentration of bilirubin is too high to be read against the standard in the colorimeter, the standard may be concentrated by adding only half the quantity of ether. In order to avoid error from evaporation of the ether standard, transference of the solution to the colorimeter should be rapid and the readings made at once.

The standard matches in color a dilution of 5 mg. per liter of bilirubin. This dilution is the standard unit in terms of which the concentration of bilirubin is stated. Thus, the amount of bilirubin in the normal serum is 0.2 to 0.6 units or a dilution of 1 to 3 mg. per liter.

The dilution of the serum in the quantitative test must be taken account of. Van den Bergh says that if 0.5 cc of serum is precipitated with 1 cc of alcohol and centrifuged the supernatant fluid is $\frac{10}{7}$ cc, or 1.43 cc. The amount of pigment left in the precipitate is not considered. The amount of bilirubin in the 0.5 cc of serum is now in the $\frac{10}{7}$ cc of supernatant fluid, and so is in a dilution of $\frac{20}{7}$. To 1 cc of this supernatant fluid is added 0.25 cc of diazo solution and 0.5 cc of alcohol making this dilution $\frac{7}{4}$. Thus the total dilution is:

$$\frac{20}{7} \times \frac{7}{4} \text{ or } 5$$

The final reading must therefore be only one-fifth of the actual amount present and must be multiplied by 5. The amount of pigment left in the precipitate is ignored. It is greater in amount in cases of obstructive jaundice to judge from the color.

In carrying out the method the writer has found that there are several important points: (1) The reagents must be fresh and of good quality (considerable difficulty occurred when sulphanilic acid, which had been in stock for some time, was used); (2) the solutions must be made up fresh after the time mentioned for each has passed; (3) the glass tubes which are used must be clean.

A number of sera were examined immediately after collection of the blood and also after twenty-four hours in the ice box. In no case was any change found in either the direct or indirect reaction. At room temperature there was a diminution in the bilirubin content after twenty-four hours. Plasma from oxalated blood was examined, using the serum as a check in several cases and the same reading obtained. In the cases here recorded the tests in most instances were made within two hours of the collection of the blood. Occasionally the specimens had been kept on ice.

Slight hemolysis does not interfere with the readings. To a number of samples of blood enough distilled water was added to cause a distinct pink color in the serum. Allowing for the dilution, these sera gave the same reading as the non-hemolyzed controls. Almost all sera will give some color in the indirect reaction. Occasionally a normal serum gives a color too slight to read, that is, less than 0.2 units or 1 mg. of bilirubin per liter, but the writer has seen only two specimens with no trace of color. The addition of the 0.5 cc of alcohol after adding the diazo solution will clear up any opacity which may be present. Any serum having a positive direct reaction will have a positive indirect reaction but the reverse is not true.

Interpretation of the Test. The direct test may result in one of three ways:

1. The immediate direct: When this reaction occurs the bilirubin is believed to be present in the form in which it occurs in the bile, hence an obstructive jaundice is indicated. In 7 cases of common duct stone, and in 7 cases of occlusion of the common duct by tumor or pancreatic disease, the immediate direct reaction occurred.

2. The delayed direct reaction and the negative direct reaction must be grouped together clinically, for either may occur when there is increased bilirubin of the non-obstructive or hemolytic type. In the anemias, in chronic cholecystitis, and usually in the infective or toxic jaundices, the reaction is of this type.

2. The biphasic reaction is apparently a combination of the two preceding reactions. There is an immediate direct reaction with later developing increase of color. The biphasic reaction occurred in this series in 2 cases of pneumonia with jaundice, 1 case of catarrhal jaundice, and 1 case of cirrhosis. It is well to point out that the absence of a biphasic reaction does not mean that only bilirubin of the obstructive form is present, for often the hemolytic form of bilirubin is present but gives no reaction by the direct method.

The amount of bilirubin present, as determined by the indirect reaction, does not determine the presence or absence of the delayed reaction, for a high indirect reading was in several instances accompanied by an absent direct reaction.

Three forms of bilirubin must therefore be distinguished: That giving the immediate direct reaction, that giving a delayed direct reaction and a third which gives no direct reaction. All three react in the presence of alcohol and give a positive indirect. The delayed direct and absent direct cannot be separated in their clinical significance, for in every pathological condition in my series of cases in which one occurred the other was also observed in 1 or more cases.

That there is a distinct difference between the obstructive pigment and the hemolytic there can be no doubt. Andrewes[9] recently has been able to demonstrate other differences than that of their reaction to the diazo reagent, but the fundamental reason for these differences is as yet unknown.

The indirect reaction is purely quantitative. All forms of bilirubin apparently react to it. The normal serum has been found to contain bilirubin in a concentration of from 1 to 3 mg. per liter, or, in terms of units, from 0.2 to 0.6 unit.

The ability to detect small amounts of bilirubin in the serum has made possible the recognition of latent jaundice and of increases or decreases in the amount of bile pigment in the blood of a patient.

Results. The results in this series of cases of chronic cholecystitis do not confirm the findings of some investigators, for 7 of the 9 cases are well within normal limits—1 is top-normal (0.6), while only 1 is above this figure. Friedman and Straus,[10] who report a series of cases of cholecystitis, using the van den Bergh reaction but without making a quantitative test for bilirubin, considered any serum giving a definite pink tint in the indirect reaction as pathological. Many sera from normal individuals have a bilirubin content of 0.4 to 0.6 unit and this means that there is a definitely pink color with the diazo reagent. A quantitative figure below 0.6 unit certainly cannot be considered abnormal.

Evarts Graham and his associates[11] have shown the relationship between hepatitis and cholecystitis. In their opinion many of the cases of cholecystitis are the result of a primary hepatitis, the liver being usually infected through the portal circulation. Since the lymphatics of the liver and gall bladder communicate with each other a primary cholecystitis may result in a secondary hepatitis, but the gall bladder may be infected primarily without extension of the process to the liver. Thus the results of the van den Bergh reaction may vary, depending upon the degree of hepatitis associated with a cholecystitis. The cases in which hepatitis accompanies the cholecystitis may explain the increase in the bilirubin of the indirect test. If the cholecystitis is primary and the liver damage slight no evidence of the latter will be found by this test.

In the cases of chronic calculus cholecystitis without obstruction of the common duct it is probable that the infection has persisted for a longer period and has so affected the hepatic cells as to cause definite damage with retention of pigment and hence high values for the indirect reaction. Of the 11 cases in the this series 5 were definitely high, 3 were top-normal and only 3 were well within normal limits.

As would be expected, the cases of common duct stone,[7] and those of occlusion of the common duct by tumor or pancreatic disease,[7]

showed high values in the indirect reaction and an immediate direct reaction due to the obstruction to the outflow of bile and consequent readmission into the blood of bile pigments.

TABLE I.

	Indirect units.	Direct.
Chronic cholecystitis	0.2	Negative
	0.2	"
	0.2	"
	0.3	"
	0.3	"
	0.4	"
	0.5	"
	0.7	"
	0.6	Delayed
Chronic calculus cholecystitis	0.2	Negative
	0.4	"
	0.5	"
	0.6	"
	0.9	"
	1.0	"
	0.6	Delayed
	0.6	"
	0.8	"
	1.1	"
	1.9	"
Acute cholecystitis	0.6	Negative

TABLE II.

	Indirect units.	Direct.
Common duct stone	2.1	Immediate
	5.0	"
	5.0	"
	5.0++	"
	8.0	"
	8.0	"
	9.0	"
Occlusion of common duct by tumor or pancreatic disease	3.6	Immediate
	18.0	"
	5.0++	"
	5.0++	"
	9.8	"
	1.4	"
	5.0	"

In pneumonia the direct reaction shows variations of especial interest. As will be seen from Table III, the majority of cases gave a delayed or negative direct reaction with, in 1 case, a bilirubin concentration as high as 25 mg. per liter (5 units). In 2 cases a biphasic direct reaction was present and in only 1 an immediate direct reaction. It is possible in the last case that the very strong immediate reaction masked a less-marked delayed one. These delayed and negative reactions point to either an active hemolysis or to a toxic condition of the liver which interferes with its normal

action upon the bile pigment. In the 3 cases with biphasic and immediate reactions reabsorption of bile has certainly occurred if we accept van den Bergh's interpretation of the immediate direct reaction.

TABLE III.

	Indirect units.	Direct.
Pneumonia	5.0+	Immediate
	9.5	Biphasic
	2.2	"
	1.0	Delayed
	5.0	"
	1.5	"
	0.75	"
	0.6	Negative
	1.4	"

The difference in the quantitative readings between the severe secondary anemias and the cases of pernicious anemia is striking.

TABLE IV.

	Indirect units.	Direct.
Primary pernicious anemia	0.4	Negative.
	0.6	"
	0.6	"
	0.7	"
	0.8	"
	0.8	"
	0.9	"
	1.1	"
	1.1	"
	1.2	"
	1.5	"
	1.7	Delayed
	1.9	"
	4.0	Negative.
Primary pernicious anemia (?)	0.2	Negative.
	0.6	"
	0.7	"
	1.0	"
Secondary anemia	0.2	Delayed
	0.2	Negative.
	0.2	"
	0.2	"
	0.2	"
	0.2	"
	0.2	"
	0.2	"
	0.2	"
	0.3	"
	0.3	"
	0.4	"
	0.5	"
	0.6	"
Hemolytic ictero-anemia	1.5	Negative.
	2.1	"
	2.5	Delayed
	4.0	Negative.
Leukemia	±0.2	Negative.
	±0.2	"
	±0.2	"
Purpura hemorrhagica	0.0	Negative.

All except one of the readings in pernicious anemia were top-normal or above normal, one as high as 4 units. In the secondary anemias, on the other hand, 9 of the 14 cases had 0.2 unit, the lowest reading possible; 2 had 0.3 and only 1 was as high as 0.6. Whatever the cause, bilirubin is increased in the blood in the primary anemias, and present in normal amounts in the severe secondary anemias.

The quantitative readings in the cases of cardiac decompensation are of interest, for of the severe cases 4 were definitely high, 1 was top-normal, while only 2 were well within normal limits. The direct reactions were either delayed or negative. The hepatic involvement commonly found in cardiac decompensation might well account for this increase of the pigment.

TABLE V.

	Indirect units.	Direct.
Catarrhal jaundice	19.5	Biphasic
	4.1	Immediate
	5.0++	"
	2.0	Delayed
	1.8	"
	3.1	"
	5.0	"
Cirrhosis	0.6	Negative
	0.45	"
	0.4	"
	2.5	Biphasic
Carcinoma of liver	0.2	Negative
	0.5	"
	0.5	"
	2.0	"
	0.8	"
Arsphenamin toxemia	1.2	Delayed
Cardiac decompensation	0.4	Slightly delayed
	0.4	"
	0.6	"
	1.1	Delayed
	1.2	"
	1.2	"

Summary. The test of van den Bergh for the estimation of the type and quantity of bilirubin found in the blood serum is discussed, as is also his interpretation of the test and the theories on which he bases his interpretation. Whether van den Bergh's theory of jaundice is accepted or not, the test and his interpretation of it are in accord with the clinical findings in a series of over 100 cases. Normal results range from 0.2 to 0.6 unit, the majority of readings being 0.2 to 0.3.

In 14 cases of occlusion of the common duct by stone, tumor or pancreatic disease, a strong immediate direct reaction was obtained and the indirect reading ranged from 1.4 to 18 units.

Serum from 9 patients with chronic cholecystitis gave only the delayed or negative direct reaction, and the indirect reaction gave a value above normal in only 1 case. Eleven cases of chronic calculus cholecystitis gave negative or delayed direct reactions, with indirect readings from 0.2 to 1.9 units.

In 14 cases of secondary anemia the indirect result was always within the normal range. In 14 cases of pernicious anemia the bilirubin in the serum was high, from 0.7 to 4 units in 11 cases; 0.6, or top-normal, in 2 cases; well within normal limits, 0.4, in 1 case.

Four cases of hemolytic ictero-anemia showed a greatly increased amount of bilirubin of the hemolytic type, in the serum, 1.5 to 4 units. In 3 cases of leukemia and 1 of purpura hemorrhagica low normal values were obtained.

Conclusions. The van den Bergh test for bilirubin in the blood serum in this series of over 100 cases has given results which are in accord with the clinical picture. These tests differentiate consistently between the jaundice of obstruction and of hemolysis.

They are tests for liver function only in so far as they indicate alteration in bile pigment metabolism.

REFERENCES.

1. Meulengracht, E.: Compt. rend. Soc. de biol., 1921, **84**, 153.
2. van den Bergh, H.: Der Gallenfarbestoff im Blute, Leiden, 1918.
3. Ehrlich, P.: Deutsch. med. Wchnschr., 1883, **9**, 549.
4. Pröscher: Ztschr. f. physiol. Chem., 1900, **29**, 411.
5. van den Bergh and Schnapper: Deutsch. Arch. f. klin. Med., 1913, **110**, 540.
6. Küpffer, C.: Arch. f. mikr. Anat., 1899, **54**, 254.
7. Aschoff, L.: München. med. Wchnschr., 1922, **69**, 1352.
8. McNee, J. W.: Quart. Jour. Med., 1922–1923, **16**, 390.
9. Andrewes, C. H.: Brit. Jour. Exper. Path., 1924, **5**, 213.
10. Friedman, J. C., and Straus, D. C.: Jour. Am. Med. Assn., 1924, **82**, 1248.
11. Graham, E. A., and Peterman, M. G.: Arch. Surg., 1922, **4**, 23.

THE THYROXIN AND TRYPTOPHANE CONTENT OF THE DISEASED THYROID GLAND, AND THE IODIN COMPOUNDS IN DESICCATED THYROID.*

By James F. Weir, M.D.,

DIVISION OF MEDICINE, MAYO CLINIC AND MAYO FOUNDATION, ROCHESTER, MINN.

When the thyroid gland is boiled with dilute sodium hydroxide, and is then made acid, about 50 per cent of the total iodin present is found in the precipitate and 50 per cent is soluble in the presence of mineral acid. The soluble iodin compounds do not possess any demonstrable physiological activity, and it is difficult to conceive

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of any chemical procedure by which they could be altered to produce thyroxin. The acid insoluble material contains all of the thyroxin which is present after boiling with alkali. Whether this is a measure of the total amount originally present cannot be determined. A large percentage of the iodin in this fraction can be separated as thyroxin without further alteration. This procedure, therefore, is a possible method of estimating the relative content of thyroxin in various samples of thyroid material.

The method which has been used is to boil, under a reflux condenser, 10 gm. of finely ground, fresh goiter tissue removed at operation, with 4 per cent sodium hydroxide for fifteen minutes, then to remove a sample, continue boiling for one hour, to remove a second sample, and continue boiling for two hours. The various samples are than treated with acid and filtered. Acid is added to precipitate thyroxin, which is insoluble in neutral or acid solutions. Iodin is determined in the solution before precipitation, and in the filtrates, by the method developed by Kendall. Samples of desiccated thyroid were similarly treated.

The author studied the goiters in a series of 37 cases, consisting of 24 of parenchymatous hypertrophy (exophthalmic goiter) and 13 adenomatous glands (Table I). The cases of exophthalmic goiter are considered first, and in the order of increasing total iodin content. Then follow cases of adenomatous goiter in the same order and without considering the presence or absence of clinical symptoms (Table II).

Wilson and Kendall have shown that in normal glands approximately 50 per cent of the total iodin is stable in boiling alkali, and is acid-insoluble. In cases of adenomatous goiter this percentage may or may not be changed. In the small series considered here the average was 52 per cent; the extremes, 15 and 66 per cent. This average is considerably higher than that reported by Wilson and Kendall, their percentage being 30 in cases with hyperthyroidism, and 34 in cases without hyperthyroidism. Neither from the thyroxin content nor total iodin content could any indication of the presence or absence or severity of hyperthyroidism be obtained. It is interesting to note, however, that in all cases in which there was high total iodin content the goiter was described by the pathologist as colloidal in type.

The hyperplastic (exophthalmic goiter) glands, as shown by Wilson and Kendall, present two changes: Low total iodin content and a low percentage of total iodin as thyroxin iodin. In their series of cases the total iodin was 0.11 per cent (1.1 mg. in each gram.), and the average thyroxin content was 28 per cent. In the 24 cases of exophthalmic goiter the average total iodin was 0.26 per cent (2.58 mg. in each gram), of which an average of 43 per cent was thyroxin iodin. Thus not only is the total iodin much higher, but also the percentage in the form of thyroxin is

materially increased. The difference in these percentages is undoubtedly due to the administration of iodin (Lugol's solution)[4] to all such patients over a variable length of time prior to operation. Thus we have a chemical criterion which agrees with the general clinical improvement of the patient.

TABLE I.—IODIN CONTENT OF GOITERS.

Case.	Diagnosis.	Basal metabolic rate.	Iodin and tryptophane in each gram of dried gland.			
			Total iodin, mg.	Iodin, stable after boiling, mg.	Iodin, stable (thyroxin), per cent.	Tryptophane, mg.
1	Exophthalmic goiter . .	+79	0.86	0.18	20	21.4
2	Exophthalmic goiter . .	+51	1.04	0.33	32	15.4
3	Exophthalmic goiter with adenoma	+73	1.25	0.40	32	
4	Exophthalmic goiter . .	+57	1.36	0.37	27	
5	Exophthalmic goiter . .	+31	1.36	0.54	40	26.4
6	Exophthalmic goiter with thyroiditis	+49	1.36	0.63	47	
7	Exophthalmic goiter . .	+26	1.45	0.15	10	
8	Exophthalmic goiter . .	...	1.80	0.70	39	
9	Exophthalmic goiter with adenoma	+28	1.90	0.30	15	
10	Exophthalmic goiter with adenoma	+49	1.91	0.70	38	
11	Exophthalmic goiter . .	+39	2.15	1.25	58	35.0
12	Exophthalmic goiter . .	+62	2.40	1.20	50	38.0
13	Exophthalmic goiter . .	+90	2.41	1.00	42	
14	Exophthalmic goiter . .	+38	2.72	0.83	31	26.6
15	Exophthalmic goiter with adenoma	+33	2.72	1.80	62	
16	Exophthalmic goiter . .	+76	2.90	1.20	42	19.0
17	Exophthalmic goiter . .	...	2.90	1.55	54	33.2
18	Exophthalmic goiter . .	+100	3.30	1.75	53	41.6
19	Exophthalmic goiter . .	+62	3.33	1.30	39	
20	Exophthalmic goiter . .	+78	3.45	1.82	53	33.2
21	Exophthalmic goiter with adenoma	+55	3.50	2.10	61	
22	Exophthalmic goiter . .	+38	3.80	2.75	73	28.5
23	Exophthalmic goiter . .	+84	5.73	2.95	52	33.3
24	Exophthalmic goiter . .	+84	6.25	3.80	61	33.3
25	Adenoma with hyperthyroidism.	+19	0.31	0.19	63	34.2
26	Non-toxic adenoma . .	− 1	0.39	0.06	15	
27	Non-toxic adenoma . .	0	0.72	0.45	63	
28	Adenoma	...	0.77	0.19	25	38.4
29	Toxic adenoma	+21	0.96	0.42	44	
30	Toxic adenoma	+35	1.05	0.33	32	
31	Toxic adenoma	+44	1.28	0.56	48	
32	Toxic adenoma	+31	1.32	0.64	49	
33	Toxic adenoma	+56	1.94	1.19	61	31.3
34	Adenoma in colloid thyroid	+19	2.58	1.16	45	33.1
35	Adenoma in colloid thyroid	+31	3.25	1.70	53	33.3
36	Toxic adenoma	+26	3.27	1.96	60	40.4
37	Toxic adenoma	+47	3.65	2.40	66	

TABLE II.—SUMMARY AND AVERAGES OF IODIN IN GOITERS.

Type of cases.	Cases.	Average basal metabolic rate.	Iodin and tryptophane in each gram of dried gland.			
			Total iodin, mg.	Iodin as thyroxin, mg.	Iodin as thyroxin, per cent.	Tryptophane, mg.
Exophthalmic goiter . .	24	+56	2.58	1.11	43	29.6
Adenoma	13	+27	1.65	0.86	52	35.1

No relationship could be established between the basal metabolism and the thyroxin content.

Because of the close structural relationship between thyroxin and tryptophane it was thought that a determination of the latter might show changes in pathological conditions. The method employed was that of May and Rose, depending on the development of a blue color with dimethylpara-aminobenzaldehyde. Casein was used as a standard, and calculations were based on casein containing 2 per cent of tryptophane. The determination was carried out on 52 glands removed at operation (Table III). The average content was 29.6 mg. in each gram of dried tissue (approximately 3 per cent). On classifying these glands according to the type of disease, clinically or pathologically, no characteristic variations are found. Furthermore, no relationship could be established between the content of thyroxin or tryptophane or the basal metabolic rate.

TABLE III.—TRYPTOPHANE CONTENT OF THYROIDS.

Milligrams in each gram.	Cases.	Exophthalmic goiter.	Adenomatous goiter.
10 to 15	2	2	
15 to 20	5	5	
20 to 25	7	4	3
25 to 30	14	10	4
30 to 35	14	7	7
35 to 40	5	4	1
40 to 45	4	1	3
45 to 50	1	..	1
	—	—	—
Total	52	33	19
Average content . . .	29.6	27.5	33.0

The Iodin Compound of Desiccated Thyroid. A specimen of desiccated thyroid was used in these experiments. Two grams were dissolved in 100 cc of water and 20 cc of 20 per cent sodium hydroxide and boiled under a reflux condenser for varying lengths of time. The specimens were then removed, neutralized with sulphuric acid, and the precipitate filtered off. It was necessary to add 200 to

300 mg. of an organic acid to the solution in sodium hydroxide before neutralizing with acid. This organic acid was insoluble in acid and would flocculate the precipitate prior to filtering. If tungstic acid instead of sulphuric acid was used, this procedure was unnecessary. Iodin was determined in the filtrates. The total iodin was 2.8 mg. in each gram. As boiling was prolonged, it was increasingly difficult to obtain a satisfactorily clear filtrate, even using tungstic acid as a precipitant (Table IV).

TABLE IV.—IODIN IN DESICCATED THYROID, SODIUM HYDROXIDE STABLE AND ACID INSOLUBLE.

Time in hours.	0.25.	1.	3.	9.
Milligrams iodin in each gram soluble in sulphuric acid . .	0.8	1.0	1.5	1.3
Per cent of iodin soluble . . .	28.5	35.7	53.6	46.4
Per cent of iodin stable in sodium hydroxide	71.5	64.3	46.4	53.6

From these figures we see that, on an average, 50 per cent of the iodin in desiccated thyroid is stable in boiling sodium hydroxide, and is insoluble in acid. Thyroxin is the chief constituent of this portion. Further decomposition of the iodin compound is not obtained by boiling for periods longer than three hours.

It is difficult to determine whether the iodin is present as an organic iodin compound or as sodium iodid after boiling in sodium hydroxide. However, the nitrous acid test gives some information. Three grams of desiccated thyroid were boiled in sodium hydroxide for one hour, cooled, treated with tungstic acid and filtered. The filtrate was evaporated to less than 10 cc, and then nitrous acid and starch were added. A good trace of blue color appeared; however, not more than was obtained with 0.1 mg. iodin in the form of sodium iodid. After boiling 3 gm. of desiccated thyroid for one hour, at least 3 mg. of iodin is soluble in mineral acids. If this was present as sodium iodid a very strong nitrous acid test would have been obtained. Evidently, therefore, the compounds which are acid-soluble contain iodin, and only a very small amount (less than 5 per cent) of the total iodin is broken off as inorganic iodids. These results show that the iodin in the thyroid is practically all in organic combination; about 50 per cent is insoluble in acid and 50 per cent is soluble in acid after the gland has been boiled in 4 per cent sodium hydroxide.

Summary. From the synthetic work with thyroxin, it appears impossible to alter any compound which could be called a precursor of thyroxin into thyroxin by treatment with alkaline hydroxide.

In the normal gland the amount of total iodin present in a form stable to sodium hydroxide (thyroxin) is approximately 50 per cent of the total iodin.

In the exophthalmic goiter the total amount of iodin present is

less than normal, and the percentage of the total which is in the form of thyroxin is very materially reduced.

After administration of Lugol's solution the total amount of iodin in the exophthalmic goiter increases, and the percentage in the form of thyroxin increases. These changes parallel the clinical improvement in the patient.

There is no apparent relationship between the thyroxin content of the thyroid and the basal metabolic rate.

Tryptophane exists in the thyroid in rather high percentage, an average of 3 per cent, but no definite relationship was found between this and the type of gland pathologically, the thyroxin content or the basal metabolic rate.

The iodin which is soluble in acid after the gland has been digested with sodium hydroxide is not present as inorganic iodid, but is still organically combined.

BIBLIOGRAPHY.

1. Kendall, E. C.: The Isolation in Crystalline Form of the Compound Containing Iodin which Occurs in the Thyroid; its Chemical Nature and Physiological Activity, Trans. Assn. Am. Phys., 1915, **30**, 420.

2. Kendall, E. C.: Determination of Iodin in Connection with Studies in Thyroid Activity, Jour. Biol. Chem., 1920, **43**, 149.

3. May, C. E., and Rose, E. R.: The Trytophane Content of Some Proteins, Jour. Biol. Chem., 1922, **54**, 213.

4. Plummer, H. S., and Boothby, W. B.: The Value of Iodin in Exophthalmic Goiter, Jour. Iowa State Med. Soc., 1924, **14**, 66.

5. Wilson, L. B., and Kendall, E. C.: The Relationship of Pathological Histology and Iodin Compounds of the Human Thyroid, Am. Jour. Med. Sci., 1916, **151**, 79.

THE USE OF LIPIODAL IN THE LOCALIZATION OF SPINAL LESIONS.

A Preliminary Study.

By Franklin G. Ebaugh, A.B., M.D.,

DIRECTOR, COLORADO PSYCHOPATHIC HOSPITAL, DENVER, COLORADO.

(From the Neuropsychiatric Department, Philadelphia General Hospital, Philadelphia.)

The use of lipiodal (iodized poppy oil), since its introduction by Sicard,[1] has been of great diagnostic value in the localization of spinal block, thereby paving the way for early operation in cases of spinal cord tumors. Ayer's[2] work regarding puncture of the cisterna magna and his elaboration of combined cisternal and lumbar punctures has made possible the diagnosis and demonstration of spinal subarachnoid block from any cause, but does not give accurate localization. The intracistern injection of iodized oil

combined with roengenographic studies will show location of spinal blocks. It is the purpose of this paper to report briefly 3 cases in which lipiodal was of great value in localization. In 2 cases its use led to operation, in which the findings of spinal block were verified. In another case the findings were negative and saved the patient from a possible laminectomy. We also wish to comment briefly upon the reactions following the injection of iodized oil, and the need for further observations concerning its routine use combined with roentgenographic studies.

Case Reports and Comment. CASE I.—J. H. H., aged twenty-five years, was transferred from the medical service, May 7, 1924, to the neurological service of the Philadelphia General Hospital, of Drs. Charles Potts and J. W. McConnell. He had had pneumonia January, 1924, followed by empyema. An exploratory thoracotomy was performed April 30, 1924. At this time spinal anesthesia was unsuccessful and a diagnosis of spinal block suggested itself. Roentgenographic studies gave evidence of fluid in the left chest. Neurological examination showed paralysis of both legs. Atrophy of both legs was marked and sensory disturbances consisted of dysthesia for pain sense beginning with the first dorsal segment and becoming more marked at the level of the fifth dorsal segment and extending to the first lumbar segment. This dysthesia without definite level together with the history of lung infection and subsequent unsuccessful attempt to institute spinal anesthesia pointed to a diagnosis of diffuse myelitis more marked between the seventh dorsal segment and the first lumbar segment. A possibility of plastic exudate about the nerve roots could not be ruled out. During the patient's course in the hospital, two combined cisternal and lumbar punctures were performed. The following data were obtained:

COMBINED LUMBAR AND CISTERNAL PUNCTURE JULY 6, 1924.

	Cisternal data.	Lumbar data.
Initial pressure	60 mm.	60 mm.
Pulse variation	Good	Slight
Respiratory variation	Good	Slight
Increase on pressure over jugular, marked	60 mm. to 320 mm.	60 mm. to 70 mm.
5 cc fluid removed from lumbar	60 mm.	35 mm.
5 cc cisternal fluid removed	50 mm.	35 mm.
5 cc fluid from lumbar	50 mm.	0

Coughing and abdominal pressure caused a uniform increase in pressure in cisternal manometer with no change in lumbar region.

Cisternal fluid: Clear; no cells; globulin, slight increase; colloidal gold, 0001110000. Wassermann negative.

Lumbar fluid: Clear, heavy; globulin, increase; colloidal gold, 5555555422. Wassermann negative.

Diagnosis of subarachnoid block was made.

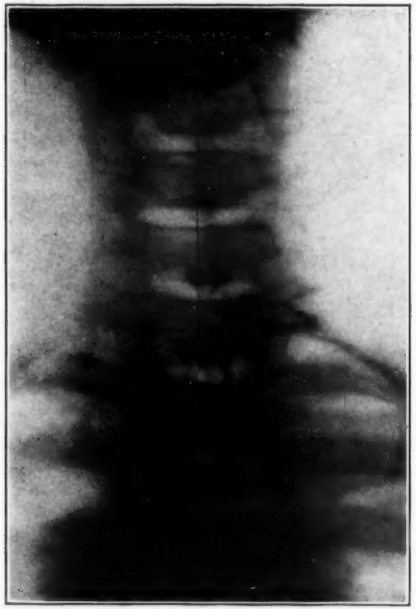

FIG. 1.—Taken one hour after injection, showing iodized oil extending from first to fifth dorsal vertebra.

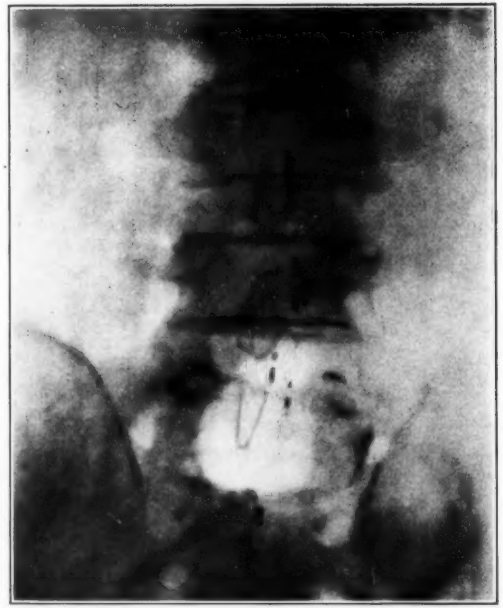

FIG. 2.—Showing location of iodized oil six hours after injection.

FIG. 3.—Showing position of iodized oil eighteen hours after injection.

FIG. 4.—Showing iodized oil at the lowest level in the subarachnoid system, demonstrating that no block was present.

FIG. 5.—Showing iodized oil at the fifth dorsal vertebra, corresponding to site of neurological diagnosis.

Combined puncture was repeated July 28, 1924, with similar readings. At this time 2 cc of lipiodal was injected in the cisterna magna. On the basis of the two double punctures a diagnosis of spinal block was made. A diagnosis of complete spinal block was not definite because in each case there was some change in the lumbar monometer on pressure over the jugulars, which we have not noticed previously in complete blocks. The roentgenographic reports* following the injection of lipiodal were as follows: The initial film (Fig. 1) taken one hour after injection shows "more than one column of the opaque material—one to the right of the spines of the vertebra extending from the first to the fifth dorsal, on the left from the first to the third dorsal. There is none of the oil below these points." Films made six hours later (Fig. 2) show "injected material on each side of the spine first and second dorsal, and disintegrated particles along the right of the spine from the first lumbar to the sacrum." The films made eighteen hours later (Fig. 3) show "similar appearances of dorsal region as in the first one made. The lumbar vertebra are similar to the second film except there is more of the oil at the sacrum." Previous roentgen-ray examinations of the spine were negative. The laboratory reports on two occasions showed negative fluid and spinal fluid Wassermann. The colloidal curve was 3455555532. Blood chemistry and other studies were negative.

A laminectomy was performed August 19, 1924, by Dr. Francis Grant under ether anesthesia. The spines of the fourth, fifth and sixth dorsal were removed. Outside of the dura considerable fluid was found. On rinsing, the dura was found to be directly against the cord without any intervening fluid. It is interesting that these findings corresponded closely to those of the initial plate, in which the iodized oil tended to localize at the fifth dorsal vertebra (Fig. 1).

This case was an extremely confusing one and the value of the use of lipiodal combined with double puncture is illustrated, the final operation showing a diffuse adherent inflammatory exudate about the spinal cord as localized by lipiodal and roentgenographic studies. The findings of complete block by the use of double puncture were also verified at operation.

Case II† may be briefly discussed, since the opinion that there was no spinal block present was confirmed following the injection 3 cc of lipiodal into the cisterna magna. The above film taken shortly after the injection shows that all the iodized oil has reached the base of the spinal sac (Fig. 4). This case was a confusing one in that at first many signs pointed to a spinal cord lesion in the lower cervical region. A diagnosis of epidemic encephalitis with radiculitis was made and has been confirmed by the later develop-

* The studies were made by Dr. Holmes of the Philadelphia General Hospital Roentgen-ray Laboratories.

† Service of Dr. C. A. Heiken of the Misericordia Hospital.

ment of a paralysis agitans syndrome. The use of lipiodal in this case not only decided the diagnosis, but probably saved the patient from an exploratory laminectomy, which would have been justified without the use of this method.

Case III is of extreme interest in that combined cisternal and lumbar puncture was not completed owing to inability to obtain fluid from the lower region. Previously the report showed a yellow fluid containing three cells with a heavy cloud of albumin. Repeated neurological examinations in this case showed evidence of localization of the tumor at the fifth dorsal vertebra. A definite diagnosis of spinal cord tumor was made, since all other diagnostic possibilities were ruled out after detailed studies. The patient had the typical sensory and motor symptoms at onset. A sensory impairment corresponding to the seventh spinal segment was evident. All laboratory examinations were negative. The Queckenstedt test showed that there was no increase in cerebrospinal fluid pressure in the lumbar area. The pressure determinations and variations in the cisterna magna were normal. Two cc of the iodized oil were injected in the cisterna magna and films taken shortly afterward showed definite localization at the fifth dorsal vertebra (Fig. 5). On April 23, laminectomy was performed by Dr. Rodman and a tumor was removed from the above location. This tumor was located on the anterior surface of the cord and was approximately 4 cm. in length. Gross appearance was that of a neurofibroma, which readily separated from the cord.

This case was interesting in that following the lipiodal injection the patient complained of pain in the seventh spinal segment and localized sweating over the adjacent vertebra was present. These phenomena disappeared twenty-four hours after the injection. On the basis of reports by Laplane[3] this pain is significant and arises apparently in the sensory roots at the point of lesion. These findings are, therefore, of clinical import and frequent neurological examinations after lipiodal injection should be made. In this preliminary report we were interested in the apparent absence of other reactions following the injection of iodized oil. There were no definite reactions. The patients objected to repeated punctures and we were unable to follow possible cytological changes following the injection of lipiodal. At present there are no reports in American literature available except the work of Ayer and Mixter[4] and this case report by Russell.[5] The work of Ayer and Mixter indicated that lipiodal causes irritation and they feel this method is not for indiscriminate use. Careful studies of spinal fluid cytology should be made as well as quantitative globulin determinations. Roentgen-ray films made several days after injection of the oil showed that there was no change in position and that the oil gravitated to the lowest point possible. Careful postmortem studies should be made regarding the possible demonstration of inflammatory reactions. In the future fluoroscopical studies should prove

interesting and should enable one to determine the time required for the passage of the oil from the cisterna magna to the sacrum, as well as the best position in which to take roentgenograms. In our studies the sitting position was used in each case. Laplane prefers the lateral decubitus on an incline, which he feels is more favorable for the passage of the oil. The application of this method should clarify and differentiate many confusing spinal lesions, particularly brought up by the question of spinal caries and extradural and intradural pressure of any type. Since it is clearly established that the operability of spinal cord tumors is much higher than that of brain tumors it is desirable that an early diagnosis be made. The use of iodized oil should result in the establishment of early diagnosis and, therefore, early operation. Frazier and Spiller[6] report the average time of two and two-fifths years before the diagnosis of spinal cord tumors is made. The further use of lipiodal in various inflammatory conditions, particularly of postmeningitic origin should prove of extreme value. On reviewing many cases of epidemic encephalitis we have examined, we cannot help but feel that lipiodal would have given us valuable clinical observations in this group of cases. At least its use would have prevented a laminectomy in one difficult case that came to the author's attention.

Summary and Conclusions. The injection of lipiodal, with accompanying roentgenographical studies, is of definite value for the accurate localization of spinal cord block. In spinal cord tumor the use of lipiodal should lead to earlier operation and in this preliminary study of 3 cases we feel its use may be further indicated to be of value in acute inflammatory conditions, such as may arise in the treatment of, or following epidemic meningitis (subarachnoid spinal block). There were no marked subjective reactions experienced in the use of lipiodal. Further studies regarding the evidence of inflammatory changes and cytological investigations of the spinal fluid will be necessary. It is logical that lipiodal should always be injected into the cisterna magna since it gravitates and seeks the lowest level and thereby localizes at any site of obstruction.

REFERENCES.

1. Sicard, J. A.; Paraf, P., and Laplane, L: Spinal Radiography by Means of Lipoidal, Presse Med., 1923, **31**, 885. Sicard and Forestier: Presse Med., 1923, **31**, 493. Sargent, Percy: Brit. Med. Jour., August, 1923, **2**, 174.

2. Ayer, J. B.: Puncture of the Cisterna Magna, Arch. Neurol. and Psychiat., 1920, **4**, 524.

3. Laplane: Le Radio-Diagnostic des Affection intra-Rachidiennes par le Lipiodal Sousarachnoidien, La Forme Pseudo-Pottique des Tumours Intra-Rachidiennes, Amedée Legrand, 1924.

4. Ayer and Mixter: Proc. Boston Soc. Psychiat. and Neurol., December 6, 1923; Arch. Neurol and Psychiat., 1924, **11**, 499–500.

5. Russell, Ethel C.: Localization of Spinal Block by Means of Iodized Oil, Jour. Am. Med. Assn., 1924, **82**, 1775.

6. Frazier, C. H., and Spiller, W. G.: Spinal Cord Tumor, Arch. Neurol. and Psychiat., 1922, **8**, 455.

AN INSTRUMENT UTILIZABLE FOR VARIOUS OPERATIONS: BLOOD TRANSFUSION, HYPODERMOCLYSIS, INTRAVENOUS INFUSION, PHLEBOTOMY AND WITHDRAWAL OF FLUIDS FROM BODY CAVITIES.

By Henry M. Feinblatt, M.D.,
Brooklyn, N. Y.

(From the Clinical Laboratory, United-Israel Zion Hospital, Brooklyn, N. Y.)

In a previous communication the author[1] described a new and simple form of apparatus for the performance of blood transfusion by the vein-to-vein method. This instrument, it is believed, reduces the difficulties of manipulation to a minimum, and at the same time obviates the possibility of a reflux of blood from the recipient to the donor. The machine consists essentially of two disks rotating one upon the other through an angle of 90 degrees, the range of motion being limited by a stop-regulator. The proximal disk is perforated to form a channel for communication with a 20-cc Record syringe; this opening may, by rotating the disks, be made to become alternately continuous with either of two similar openings in the peripheral disk for the inlet and outlet respectively. The inlet and outlet tubes are connected, one with the donor and the other with the recipient. The machine, with the inlet and outlet projecting upward, may be held in a slotted holder, which is clamped to the table.

The purpose of this report is to call attention to some additional diagnostic and therapeutic procedures for which this instrument may conveniently be employed. In general, where it is desired to remove fluid from a patient, or to inject liquid or air, the use of this apparatus would appear to be applicable. The machine has been tried clinically and found to be useful in the following therapeutic and diagnostic procedures: (1) Hypodermoclysis, when it is desired to introduce a large amount of fluid in a short space of time; (2) intravenous infusion; (3) phlebotomy; (4) removal of fluid from the chest and abdominal cavities. In addition, several experiments on animals have indicated that a simple method of inducing artificial pneumothorax may be available by the use of this apparatus, but the author is not yet prepared to report finally upon this application.

Hypodermoclysis. The author's blood-transfusion apparatus offers a ready means of introducing considerable quantities of fluid under the skin within a short period of time. Fluids, and water in particular, are readily absorbed from the submammary

[1] Feinblatt, H. M.: A Simple Apparatus for Blood Transfusions, Med. Jour. and Record (awaiting publication).

region, the axillæ or the flanks, and it has been found that a subcutaneous injection of 500 cc can be very rapidly made.

The apparatus (Fig. 1), in addition to the transfusion instrument, consists of a 500- or 1000-cc flask, plugged with a cotton stopper around which passes a rubber tube to enter the bottle. This tube is connected with one of the terminals of the instrument by means of an adapter. The other terminal is connected directly with the needle. When it is desired to use both breasts or axillæ simultaneously, a Y-shaped connection may be utilized. The hypodermic needle should be about 3 inches long, preferably a gauge No. 18.

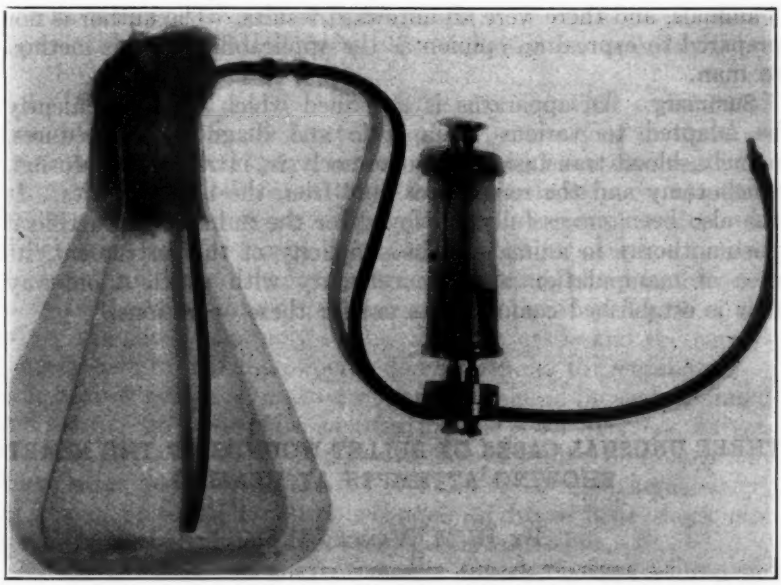

FIG. 1.—The author's transfusion apparatus adapted to the performance of hypodermoclysis.

The operation is exceedingly simple. All that is necessary to transfer the communication from the receptacle to the patient, and *vice versa*, is to rotate the disks one upon the other. The instrument is turned so that the inlet, that is, the opening in continuity with the receptacle, communicates with the syringe, and the piston of the latter is withdrawn, filling the syringe with the fluid. The disks are then rotated so as to connect the syringe with the outlet, and the syringe is emptied.

The speed of the injection is guided by the rate of absorption, as evidenced by the amount of swelling and the degree of pain induced. Bartlett[2] has shown that the addition of novocain to the solution in such amount as to produce a concentration of 0.0625 per cent

[2] Painless Hypodermoclysis, Ann. Surg., 1921, **73**, 161.

renders hypodermoclysis perfectly painless and is at the same time safe. When continuous hypodermoclysis is required, the gravity method should be employed.

Artificial Pneumothorax. Artificial pneumothorax was induced in 2 normal guinea-pigs and 1 healthy dog, injecting 40 cc of air into the such of the former animals and 120 cc into the latter. A water manometer, which could be disconnected by means of a clamp, was connected with the proximal tube of the instrument, so as to indicate, by the negative pressure induced, the entry of the needle into the pleural cavity. Ordinary atmospheric air was employed. Pneumothorax was thus successfully induced in the 3 animals, and there were no untoward results. The author is not prepared to express an opinion as the applicability of this method to man.

Summary. An apparatus is described which can conveniently be adapted to various therapeutic and diagnostic procedures, namely, blood transfusion, hypodermoclysis, intravenous infusion, phlebotomy and the removal of fluid from the body cavities. It has also been successfully employed for the induction of artificial pneumothorax in animals. The simplicity of the instrument, its ease of manipulation and the certainty with which a one-way flow is established commend its use for these operations.

THREE UNUSUAL CASES OF BULLET WOUNDS OF THE HEART SHOWING ATTEMPTS AT HEALING.

By B. M. Vance, M.D.,

ASSISTANT MEDICAL EXAMINER, CITY OF NEW YORK.

When wounds of the heart were mentioned in the writings of classical antiquity and the middle ages, the inevitable fatality of these injuries was chiefly emphasized. The possibility of healing seems never to have been considered until J. Hollerius (1498 to 1562) advanced the theory that a spontaneous cure of a cardiac wound might occasionally occur. Later several observations were published which seemed to give support to his opinion.

As an example, J. C. Weber, about 1600, described a bullet encapsulated in the heart of a stag. Idonis Wolf, in 1642, tells of a soldier whose heart at autopsy showed a healed scar at the apex, presumably the result of a sword wound received four years previously. Henri ab Heers, in 1647, writes of a man who lived seven days after his heart had been penetrated twice by bullets. Similar cases continued to be published and it soon became evident that cardiac wounds were not invariably fatal.

George Fischer, in 1868,[1] was probably the first to make an extensive attempt to review the literature of this subject. He gathered together some 452 cases of which 401 were heart wounds and 51 involved the pericardium alone. He estimated that 30 per cent of the latter and 10 per cent of the former tended to undergo spontaneous cure. Fischer's statistics include all sorts of heart injuries.

For the purpose of greater convenience it is desirable to classify wounds of the heart, and accordingly we may separate them into four main divisions:

1. Injuries caused by non-penetrating blunt force applied externally.
2. Stab wounds and cutting wounds.
3. Injuries caused by foreign bodies other than missiles.
4. Missile wounds.

1. The injuries due to blunt force show a wide variation of anatomical lesion, as the force may be a tremendous one such as an automobile wheel that crushes in the chest, or a comparatively slight grade of violence as a plank thrown from a circular saw which strikes the breast sharply in the precordial region. In either event the force acts on the chest wall in such a way that the heart is either crushed, torn or ruptured and death occurs inevitably in the vast majority of cases. From the very nature of the injury the shock is usually of such extreme grade and the hemorrhage so severe that the patients do not respond to treatment.

2. Stab wounds and cutting wounds are caused by sharp pointed and sharp edged weapons, penetrating the heart (daggers, knives, hatpins, and so forth). The resulting injury may be a huge cut that causes death in a very few minutes from rapid hemorrhage, or it may be a small wound accompanied by so little shock and hemorrhage that ultimate recovery is not impossible.

3. The queerest category of cardiac injuries is that caused by foreign bodies other than missiles, a group which includes pins, needles, nails, toothpicks, glass splinters, false teeth, and so forth. These objects are supposed to reach the heart in three ways.

The first is by penetration of the chest wall in such a manner that the foreign body will either enter the heart muscle directly or temporarily lodge in the chest wall and finally reach the heart by "wandering." This latter process is supposed to be an attraction exerted on the object by the cardiac and respiratory movements, so that it is gradually drawn to the cardiac region. In general the foreign bodies that are subject to wandering are such objects as pins and needles which have a sharp point, a slender body, and a smooth surface (D. G. Zesas[2]).

The second way in which a foreign body can reach the heart is through the gastrointestinal tract. The heart is either penetrated directly through the pharynx, esophagus or stomach or, as in the case of Bailey,[3] indirectly. Here the foreign body, a toothpick,

entered the inferior vena cava from the duodenum and was finally carried to the right auricle in the venous blood stream.

Buchanan,[3] described a third method of approach in a peculiar case in which a needle was aspirated into the air passages and finally reached the heart through the right bronchus. This method, however, is rather rare.

The symptoms evoked by such foreign bodies vary greatly. Primary symptoms may be slight or absent, and the object may be encysted in the heart, remain quiescent during life and only be discovered accidentally at autopsy. In other cases the foreign body may give rise to alarming symptoms and cause death by hemorrhage and septic infection.

4. The heart may also be wounded by missiles or projectiles, which can be defined as foreign bodies driven to their objective by a force applied at a distance. For all practical purposes in our day these terms can be limited to objects propelled by explosives, such as bullets, shrapnel, shell fragments and the like. As the driving force behind projectiles is invariably tremendous, the wound of the heart is unusually severe and the resulting shock and hemorrhage are generally rapidly fatal. A high percentage of the cases die before surgical aid can be rendered.

The primary symptom of most bullet wounds of the heart is profound shock and collapse and the individual when shot generally falls, and is unable to move. Some exceptions occur. Cases have been recorded where an individual so injured was able to do some very surprising things. In the case of Th. Muller,[4] for example, a fifteen year old boy climbed a flight of stairs immediately after his heart had been wounded by the bullet from a small caliber pocket pistol. Curran[5] also tells of some very remarkable examples of a similar kind.

The complication which accompanies the shock is hemorrhage, which may be rapid and overwhelming or gradual and slow, depending on the size of the wound, the portion of the heart involved and numerous other factors. The bleeding at first extends to the pericardial cavity, then may involve the pleural cavity and only in a few instances exudes from the external wound or extends through the diaphragm. If the blood has no means of escaping from the pericardial sac death may ensue in a few minutes from compression of the heart or heart tamponade (a true example of asphyxia). Sometimes when the pericardial wound is so placed that the blood will find an outlet into one of the pleural cavities death may be postponed for many hours. The overflow into the pleura relieves the pericardium from a dangerous rise of internal pressure, and allows the patient to live until he finally dies from mere loss of blood. Recently the author saw such a case where a man aged twenty-one years, wounded in the left lung, the pericardium, the coronary venous sinus and both auricles by a 38 caliber lead bullet, was

enabled to survive these appalling injuries about twenty-four hours, simply because he had a wound of the pericardium that drained the blood into the left pleural cavity.

In those cases where the patient lives for a number of days death may be the result of a secondary septic infection, such as pericarditis, empyema, pneumonia or general sepsis of any variety. Sometimes the exitus is due to wounds of adjacent viscera as a pneumothorax which may complicate perforation of the lung or a peritonitis complicating an abdominal injury.

A large percentage of bullet wounds of the heart tend to heal up spontaneously and Fischer's[1] estimate of 10 per cent recovery under expectant treatment is generally considered correct. The readiness with which healing takes place depends on the nature of the cardiac injury. A large missile that traumatizes the muscle and leaves a gaping hole does not allow as much chance of successful healing as does a smaller projectile which causes a small wound, and so produces less shock and hemorrhage.

The location of the wound in the heart has a very important bearing on the prognosis. Wounds of the left ventricle have the lowest mortality, wounds of the right ventricle rank next, while wounds of the auricles are the most fatal of all. This is probably explained by the fact that the thicker ventricle muscle allows the projectile more readily to penetrate obliquely without cutting across the fibers, while the thin auricle wall is usually pierced rectangularly and the fibers cut crosswise, so that the bleeding is less likely to be checked. A missile that penetrates the heart cavity or pierces a large coronary artery is much more dangerous than one that involves the myocardium alone, for the same reason. Strangely enough a rather deadly type of bullet wound is that kind which ruptures the heart without penetrating the pericardium. The missile is often spent and stops just on the outside of the pericardium or it passes over the sac tangentially "creasing" the heart, but not entering the pericardial cavity. The mechanism is exactly similar to the rupture by blunt force.

Healing when it occurs takes place in the heart just as it does elsewhere in the body. The wound is first plugged by a blood clot which is later replaced by granulation tissue and then by scar tissue. The only difference, according to Anitschkow,[6] is the presence of a large cell with a peculiar nucleus which he called a myocyte, claiming that this cell is peculiar to granulation tissue in the myocardium. In any event, the result of the process is a dense fibrous callus which effectually closes the defect in the heart wall. However, even during healing a fatal accident sometimes occurs. In the early stages an increase in the intracardiac pressure may force apart the edges of the wound causing a secondary hemorrhage. If the wound is healed the same factor may cause the formation of a cardiac aneurysm at the site of the scar. In other cases one of the

valves may be injured and a stenosis and insufficiency result which might be the real cause of death. (Klose.[7])

A large number of the cases which recover show the projectile embedded in the heart muscle enclosed by a fibrous capsule, and are often discovered quite by accident in the progress of an autopsy; for, like any other foreign body, when once encapsulated they rarely cause symptoms. Exceptions do occur, however, as in a case where the bullet by involving the bundle of His in the scar tissue gave rise to the symptoms of heart block. Aneurysm of the heart wall and adhesion of the heart to the pericardium may also result from the irritation set up by an embedded projectile (Klose[7]).

Sometimes bullets become attached to the endocardium or the pericardium. Riethus[8] has described cases in which the bullet has entered the heart cavity by penetrating the myocardium direct or by penetrating a vein and being carried to the heart by the blood.* Here the foreign body is thrown around by the blood stream until it becomes attached to the wall by fibrin which later becomes organized. Apparently while the ball is free in the blood the patient may show many signs of cardiac irritability but these disappear when it becomes attached to the endocardium.

Missiles which gain admittance to the blood stream are sometimes described as being dangerous to life, because of the possibility of embolism either from thrombi formation or because the bullet itself acts as an embolus. Sudden death in one case was caused by a projectile entering the left ventricle and then being carried by the blood to block the ascending aorta. Cases also have been described where the bullet has entered the right side of the heart or one of the systemic veins, and was later driven into the pulmonary artery with rapidly fatal results (Klose[7]).

In recent years operative repair of heart wounds or cardiorrhaphy has been extensively developed. Rehn[9] in 1896 performed the first successful operation of this kind on man, though previous unsuccessful attempts had been made by other surgeons and a suitable technic had also been worked out by animal experiments. Since then other surgeons have imitated Rehn with greater or less success. The war of 1914 to 1918, however, brought the procedure into almost common use and in place of merely suturing wounds in the heart wall, many operators have gone so far as to remove foreign bodies from the interior of the heart and on occasion to operate twice on the same heart. W. R. Smith[10] believes that cardiorrhaphy has

* The editor has offered an additional curious example of survival with a bullet in the heart. On examining the heart of an apparently normal moose that had just been shot, a mushroomed rifle bullet of larger caliber than he was using was found free in the cavity of the right ventricle. Presumably the animal had survived a previous wound, in which the bullet had entered a large vein and been swept into the right side of the heart, where it acted for an indefinite period as a ball thrombus. Its rougher edges were smoothed off with fibrinous deposits. No portal of entry was found on the body or after careful examination of the excised heart.

markedly decreased the mortality of heart wounds; he estimates that probably 1 in 10 recover under expectant treatment, while 1 out of 2 cases get well when the operation is performed.

The 3 cases presented here are some that came to autopsy in the routine work of the Medical Examiner's Office of New York City. They demonstrate very strikingly the characteristics of the kind of bullet wounds of the heart that allows the patient to survive several days or longer.

Case Reports. CASE I. T. H., aged forty-one years, a strong, well developed, white man was shot three times in the back. About fifty minutes afterward, the ambulance took him to the hospital, where he was admitted in a state of shock, but conscious and rational. He showed considerable abdominal discomfort, his skin was pale and his breathing was shallow and rapid. Physical examination then disclosed three bullet wounds of entrance in the back, and the presence of a paralysis and a loss of sensation in that part of the body below the sixth dorsal vertebra.

He was operated on that same day under local anesthesia with the result that one bullet was removed from the left axilla and another, which had injured the spinal cord, was removed from the dorsal region of the spine by a laminectomy of the sixth and seventh dorsal vertebræ.

The patient survived the injury seven days with no improvement of his paraplegia and no alleviation of his abdominal distress, which was so acute that daily gastric lavage was necessary. During his entire illness he had a daily temperature of 99 to 101° F., accompanied by rapid pulse and respirations.

Autopsy was performed about thirty hours after death. The body was that of a large well developed adult male about 5 feet 10 inches in height. His skin had an icteric tinge; there was also a superficial bedsore in the sacral region. Bullet hole No. 1 was situated in the mid-thoracic region near the spine, not far from the laminectomy incision through which the bullet had been removed at operation. Bullet hole No. 2 was found alongside of the left axilla near another operative incision. Bullet wound No. 3 was located in the lower part of the left chest posteriorly at the level of the tenth interspace, 4½ inches to the left of the spine.

On section, it was discovered that the bullet, 32 caliber lead, which made wound No. 3, passed through the left chest upward, forward, and to the right, fracturing the left eighth rib in the axillary region, perforating the left lung and the pericardium, wounding the heart and finally lodging in the upper lobe of the right lung. Both lungs showed an extensive pneumonic consolidation; the right lung was adherent to the chest wall. The left pleural cavity, however, contained 950 cc of dark fluid blood presumably due to the bullet wound of the left lung.

The pericardial cavity was of normal size and contained neither blood nor fluid. The pericardial wounds seemed to be healed. The muscle was moderately contracted but otherwise natural. Valves, aorta and coronary arteries showed nothing unusual. The heart wound was seen to be a small bluish red tunnel of the left ventricle 1½ inches in length and about ⅜ of an inch in diameter. The bullet had entered the muscle of the left ventricle near the left border and traveling forward and upward had emerged from the myocardium of the right ventricle near the septum. The cavity of the heart had not been entered nor had any important vessel been injured by the bullet.

CASE II.—H. R., aged twenty-three years, during a quarrel was shot once in the left chest anteriorly. He immediately lost consciousness but recovered rapidly. Shortly after this he was admitted to the hospital ward, displaying signs of severe shock. Examination disclosed a bullet hole in the left chest situated about the level of a line drawn between the nipples and between the left nipple and the sternum. There was no wound of exit. Subsequent roentgen-ray examination located the bullet in the spinal column about the level of the seventh dorsal vertebra.

From the very start indications were not lacking that the spinal cord was injured at the level of the seventh dorsal spine, as sensation was disturbed and the muscles were paralyzed below that point, and incontinence of urine and feces was present. Three days after the injury, bedsores developed in the gluteal regions. The neck was rigid and the spinal fluid acquired by lumbar puncture contained blood cells. The blood count showed 19,000 white cells of which 86 per cent were polymorphonuclear leukocytes. The urine merely showed a few hyalin casts, a few white cells and a trace of albumin. There were also signs of fluid in the right chest.

The patient survived the injury eight days, with a consistently high temperature of 103° F., but showing a normal pulse and respiration rate until just before his death. Then he suddenly became markedly dyspneic and cyanotic, and died in the course of several minutes.

Autopsy was performed about fifteen hours after death. The body was that of a well developed young adult male, aged twenty-three years, 5 feet 8 inches tall, weighing 142 pounds. There were numerous bedsores over the sacrum, buttocks and heels.

There was a bullet wound of entrance on the front of the left chest, very small, about $\frac{2}{10}$ inches in diameter, located 2 inches to right of the left nipple and slightly above its level. The bullet then penetrated through the fourth left costal cartilage, perforated the pericardium, heart, thoracic aorta, finally entering the thoracic spine. The bullet, a 25 caliber yellow metal jacketed bullet, was found in the spinal cord at the level of the seventh dorsal segment.

The renal pelves and the bladder showed a definite inflammation of the mucous membrane as the result of this spinal injury.

There was an enormous hemorrhage in the posterior mediastinum which projected as a huge retroperitoneal hematoma into the right pleural cavity. The pleura here had been split and the right pleural cavity contained a large quantity of blood and blood clot so that the right lung was forced over toward the left. The left lung was edematous and adherent to the chest wall by easily detached fibrinous adhesions. Neither lung was wounded by the bullet.

A pericardial perforation was found. The pericardium contained about 250 cc of blood, which was from a recent rupture, as the serous surface was not covered by any fibrinous deposit. The heart was normal in size and contracted, showing a bullet wound through the anterior surface of the right ventricle just below the ring, with perforations of the pulmonary artery, one of the pulmonary cusps, the left auricle and the thoracic aorta. The source of the pericardial hemorrhage was a recent separation of the edges of the right ventricle wound, presumably because of some sudden rise of intracardiac pressure, which the newly formed granulation tissue was unable to sustain. Sudden death therefore resulted from the rise in pericardial tension, due to the hemorrhage into the pericardial sac from the small recent perforation on the anterior surface of the right ventricle. The other in and out wounds of the auricular septum and of the left auricle were closed.

CASE III.—E. W., a young colored man, was found in a cellar unconscious and smelling strongly of alcohol. He was removed to a hospital and died there three days later, never having regained consciousness.

Autopsy showed a young colored male, aged twenty-two years, 5 feet 11 inches tall, weighing 161 pounds. Death was found to be due to a fractured skull, a lacerated brain and an extensive bronchopneumonia, secondary to the head injury. During the course of the autopsy, however, it was discovered that the deceased had evidence of an old bullet wound of the heart and the right lung probably of several years duration.

Two circular scars on the inside and outside of the biceps area of the right arm, each about $\frac{1}{2}$ inch in diameter, a similar scar on the right chest immediately over an old fracture of the seventh rib, a cord-like scar of the lower lobe of the right lung, and finally the heart lesion itself indicated clearly enough the course of this old bullet wound.

The missile had evidently entered the pericardium on the right side, but at autopsy there was no trace of such a wound. Over the most dependant portion of the right auricle was a circular fibrous scar $\frac{3}{8}$ inch in diameter, which occupied the entire thickness of the auricle wall, for it was visible on the epicardial and the endocardial

surfaces. This was evidently the point where the bullet entered the heart, penetrating about ¾ inch, to lodge finally in the muscle of the right ventricle, just below the ring and just under the epicardium where it was plainly visible. (See Fig. 1.) The bullet, 38 caliber lead, was enclosed in a thick fibrous capsule.

Photograph of the heart in Case III showing the encapsulated bullet.

There was no reason to believe that the deceased suffered any untoward symptoms because of its presence in his myocardium, where it had obviously been for a very long time. Subsequent investigation failed to establish any reliable history of the old shooting, but it was suspected that the deceased was identical with a certain negro who had been shot three years before. Positive identification was impossible because of the fondness of the dead man for aliases.

Discussion. The three cases presented here are of value in that they suggest conditions under which healing can take place in the heart wall. In Case I, a 32 caliber bullet without penetrating the heart cavity cut a tunnel in a segment of the heart muscle that was not unduly vascular. There was practically no hemorrhage into

the pericardial cavity and death seemed to be due to the spinal cord lesion and the lobar pneumonia. In Case II the heart and aorta were perforated by a small 25 caliber bullet in such a manner that bleeding was slight at the start, the patient experiencing no trouble from his cardiac injury until eight days afterward when the edges of the wound were suddenly forced apart and death resulted from the sudden hemorrhage into the pericardium. In Case III, the remarkable feature was the encapsulation of the bullet in the right ventricle with healed scars of the right auricle and the right lung, demonstrating the manner in which the bullet had reached its final resting place many years before. Death in this case was due to a recent injury which had no connection with the old bullet wound. In all three cases the bullets left wounds of such a nature in the heart that the primary complications were avoided and conditions were favorable for the process of repair.

These cases are rather unique in comparison with the other bullet wounds of the heart that have come under the observation of the Medical Examiner's office, most of which die very rapidly after the shooting. Occasionally a cardiac wound is found in a person living a few hours to two days after the injury, such as when the accompanying pericardial wound drains the blood into the pleural cavity and prevents a rapidly fatal increase of intra-pericardial pressure. It is rare however to find bullet wounds of the heart that allow any longer survival and exceedingly rare to find one that undergoes spontaneous cure, as in Case III.

It is probably true that most of the previous statistics concerning the mortality of these injuries err somewhat on the side of optimism. Immediately fatal cases are rarely published and are thus overlooked. In addition, many chest wounds that recover without operation are often erroneously diagnosed as cardiac wounds by mere clinical observation, which in itself alone cannot determine the actual state of affairs inside the chest with any degree of certainty. Consequently to compile statistics under such conditions may be misleading and give rise to erroneous interpretations.

This does not diminish the value of the fact, however, that some bullet wounds of the heart do tend to undergo spontaneous healing and that others may be amenable to a suitable operation, a knowledge which is not only of importance to surgeons but to practitioners of forensic medicine. Not infrequently vital points of evidence in homicide cases can be made clear only by appreciating the fact that a cardiac wound need not necessarily kill outright and that the patient can under suitable circumstances survive the shooting for a considerable length of time.

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REFERENCES.

1. Fischer, G.: Arch. f. klin. Chir., 1868, **9**, 561 (older literature).
2. Zesas, D. G.: Fortschritte der Medizin, 1910, **28**, 648.
3. Bailey, C. H.: Arch. Int. Med., 1913, **11**, 440. Bailey also quotes Buchanan, Tr. Path. Soc., London, 1866, **17**, 87.
4. Muller, Th.: Munch. med. Wchnschr., 1914, **61**, 1679.
5. Curran: Lancet, April 9, 1887, **1**.
6. Anitschkow: Ziegler's Beiträge, 1913, **55**, 373.
7. Klose, H.: Arch. f. klin. Chir., 1923, **124**, 210–257 (literature).
8. Riethus, O.: Deutsch. Ztschr. f. Chir., 1902, **67**.
9. Rehn, L.: Arch. f. klin. Chir., 1907, **83**, 723, Arch. f. klin. Chir., 1897, **55**, 315.
10. Smith, William Randolph: Ann. Surg., 1923, **78**, 696.
11. Giercke, H. W.: Veroffentlichungen aus dem Gebiete der Kriegs und Constitutions-Pathologie, 1920–21, **5–9**. (Literature.)

HEART BLOCK OF UNUSUAL ETIOLOGY.

BY NORMAN E. CLARKE, M.S., M.D.,
AND
F. JANNEY SMITH, A.B., M.D.,
DETROIT.

(From the Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.)

THE occurrence of heart block is now rarely of sufficient interest to occasion comment. Its presence invariably means partial or complete destruction of the auriculoventricular pathway of conduction, provided toxic causes, such as digitalis, are excluded. It occurs usually in elderly individuals whose hearts show advanced myocardial degeneration and is in most instances a permanent condition.

We have recently observed two patients suffering from this disturbance, in whom the condition arose from a very unusual etiology. The association of heart block with gumma of the septum is exceptional. In a recent paper by Major[1] he was able to find but twelve such cases reported up to 1922.

Case Reports. CASE I.—A housewife, aged thirty-five years, entered the Henry Ford Hospital on April 13, 1924, complaining of severe dyspnea and precordial pain. During the preceding three years she had suffered from slight fainting attacks which occurred at irregular intervals. She always was aware of the approach of one of these attacks by everything becoming blurred,

breathing dyspneic and the necessity for her to sit down in order to avoid falling. Complete consciousness was never lost, but there was inability to move or talk during the attack. A year previously there had appeared in her left arm and shoulder and over the precordium momentary fleeting pains of great severity. These pains were not associated with fear of death or induced by exercise. In spite of these symptoms her general health had remained fairly good, and she had been able to continue with her housework until November, 1923. She had partaken of an unusually heavy meal, when suddenly there occurred a severe pain about her heart and she lapsed into unconsciousness which lasted several minutes. From then on her dyspnea was pronounced, and within a short time edema appeared in the extremities, which symptoms steadily increased in severity and extent. The most striking feature at this time was her recognition of the fact that her heart rate had become very slow. During the three weeks previous to her admission to the hospital there had been extreme edema, ascites and orthopnea.

Her past history was essentially negative.

Physical examination showed a short, obese, young woman. The pupillary reaction to light and the tendon reflexes were prompt and normal. There was marked dyspnea and slight cyanosis. The veins of the neck were engorged, and a systolic pulsation could be felt in the suprasternal notch. The apex impulse was visible in the fifth space, 11 cm. from the midsternal line. The retrosternal dulness was increased, and tubular breath sounds were audible in this area. The heart rate was 48, the rhythm being slow and regular and the first sound at the apex muffled. The pulmonic second sound was very accentuated and distinctly reduplicated. At the apex and base there was a rough systolic murmur and a blowing diastolic murmur was heard along the left sternal border, the latter transmitted into the great vessels of the neck. Blood pressure was 190 systolic and 70 diastolic. There was congestion of both lung bases and extreme edema of both extremities. The blood Wassermann test was 4+.

During her brief stay in the hospital she had rapidly increasing decompensation. A few days before her death thrombosis of the left brachial and internal jugular vein occurred, with the production of local heat, tenderness, swelling, pain and intense cyanosis of the left arm. Death came with sudden increase in the dyspnea, intense cyanosis and collapse.

The initial electrocardiographic tracing made immediately after admission is shown in Fig. 1. The complexes were of low voltage with a *Q–R–S* interval of 0.12 to 0.16 of a second. There were notched and splintered *R* and *S* waves, flat *T* waves in Lead I, and inverted *T* waves in Lead II. The curve likewise showed complete heart block. The curve obviously showed severe myo-

cardial damage with destruction or blocking of the auricular ventricular pathway. The impulses appeared to arise in the left branch of the His bundle below the area of destruction. The later curves continued to show similar findings.

Report of Necropsy (Dr. Hartman): The heart was enlarged, weighing 550 gm. The wall of the right coronary artery was thickened, the lumen being partially occluded. The intima of the aorta showed numerous puckered, wrinkled thickenings with but few areas that were not so involved. There were no areas of calcification. The ascending portion of the aorta showed the most pronounced changes, but these pathological areas were present to a less degree in the larger branches. The aortic wall was thickened, and there were yellowish streaks of necrotic tissue between the media and the interna.

On opening the heart the chambers appeared dilated; the walls were thinner than normal. None of the valve leaflets were thickened, nor did they show any unusual changes. The ventricular septum showed a mass which bulged outward into both ventricles. This mass involved the auriculoventricular node and extended downward toward the apex for a distance of 6 cm., leaving only the apical half of the septum uninvolved. This new septal tissue was firmer and more resistant than normal, and in a section cut between the sinuses of Valsalva and downward toward the apex a change was noted from heart muscle to firm tough yellowish-gray tissue. The two endocardial surfaces were unaltered. The mass showed areas of yellowish necrotic material alternating with the grayish fibrous strands. The microscopical sections taken from the interventricular septum through the area of softening showed the muscle to be largely replaced by fibrous connective tissue, and the little muscle that remained was infiltrated here and there by round and wandering cells. In the immediate vicinity of the caseous area there was an intense infiltration by round and wandering and plasma cells. The area of destruction shaded gradually into the surrounding fibrous tissue and muscle, and about it was a zone of intense infiltration gradually changing from cells which stained well to those which stained a homogeneous dirty blue color with fragmented nuclei scattered throughout. Stains for spirochetes were made after the method of Warthin and Starry, and showed an occasional Treponema pallidum, identified by its size and short curves. Further sections through different areas of the interventricular septum were examined. These showed larger and smaller areas of round-cell and plasma-cell infiltration and areas of homogeneous dirty blue staining tissue much as previously described.

Our second patient presented numerous points of interest. The duration of his heart condition, the presence of a possibly associated gall-bladder infection, and ultimate recovery after the

operative removal of the abdominal lesion, constitute an experience which is not common among patients classified as heart cases.

CASE II.—This man, aged thirty-five years, first came under observation in our out-patient department in December, 1922. He complained of frequent colds, headaches, spells of weakness and occasional night sweats, with a slight daily rise in temperature. He had had typhoid fever several years previously and his general health had not been up to par since that time. The heart showed regular rhythm, a rate of 80 and sounds of good quality. There were no cardiac murmurs. The blood pressure was 100 systolic and 58 diastolic. Repeated physical examinations of the chest, together with roentgen rays, ruled out as far as possible any probability of pulmonary tuberculosis. He had definite involvement of the maxillary sinuses with chronically infected tonsils. A complete gastrointestinal examination revealed evidence which strongly suggested disease of the gall bladder.

In May, 1923, his heart was again examined with apparently normal findings. His spells of weakness and headaches still continued. From this time until March, 1924, he was under treatment for his constipation and chronic cholecystitis.

In March, 1924, he came to the hospital suffering from acute heart failure. He stated that ten days previously, while returning from lunch, he had climbed some stairs with comparative comfort. When he reached the top landing he saw black spots before his eyes and he suffered a feeling of faintness. On attempting to push forward he became very dyspneic, had a sense of suffocation, and it was necessary for him to sit down and rest. During the afternoon he had a similar attack of suffocation and a feeling of pounding in the region of his heart. These attacks had occurred daily up to his admission to the hospital. On a previous day, while walking a distance of about one mile, he had suffered frequent attacks which necessitated staggering to a tree or other support until he could regain his breath and balance. He described the feeling in his head as of "something rushing up into my skull and dilating my brain."

Examination. He was seen immediately after entering the out-patient department by one of us (N. E. C.). Heart failure was present with extreme cyanosis, dyspnea, moderate orthopnea and slight edema of the extremities. The heart rhythm at that time was absolutely irregular. While under examination the patient informed us that the extreme palpitation had suddenly stopped. He was sent to the "heart station" and an electrocardiogram was taken (Fig. 2). During his stay in the hospital he showed a slight elevation of temperature every three or four days. Fluoroscopical examination of the chest showed the heart to be slightly enlarged with slight prominence in the left auricular region.

An examination made after many days' rest in the hospital showed the following findings: There was palpable enlargement of the postcervical glands and moderate cyanosis of the lips. The maximum apex impulse was in the sixth interspace 9 cm. from the midsternal line inside the nipple line. The heart's rate was 80. The rhythm was regular with occasionally what appeared to be dropped beats. The sounds at the apex were only fair and rather distant. The second aortic sound was unusually accented, hollow and rather bell-like. The peripheral arteries were not palpable. The blood pressure was 105 systolic and 65 diastolic. The lungs were clear. The blood Wassermann on repeated examinations was always negative, and the spinal fluid was normal in all tests. He felt definite tenderness over McBurney's and Morris's point, but none over the gall-bladder region. There was no jaundice.

He remained in the hospital at absolute rest for about ten days, and when discharged had recovered from his acute symptoms. At this time he was advised to have an operation for the removal of his infected gall bladder.

On May 5, 1924, he was operated upon, and the appendix and gall bladder were removed. Pathological examination, by Dr. Hartman, showed the usual evidence of a chronic infection of these two organs.

He made an uneventful recovery from the operation. The constipation has persisted but the headaches have been almost completely relieved, and the heart has been so improved that at present he has none of his previous cardiac symptoms. He is symptomatically cured and is again able to carry on his daily work without difficulty. Since the operation he has gained 20 pounds in weight.

Electrocardiographic Examination. The first electrocardiogram (Fig. 2), taken in March, 1924, showed partial heart block with a P–R interval of about 0.34 seconds and large P waves in Leads II and III, probably due to auricular engorgement.

On April 1, 1924, the electrocardiogram (Fig. 3) showed complete A–V dissociation, with a ventricular rate of 58 and an auricular rate of 112. The P waves were not as prominent as they had been in the previous tracing. At this time the patient was exercised, but this had no effect whatever on the P–R interval, but did increase the ventricular rate, causing a frequent summation of the P and T waves. The administration of amyl nitrite caused results similar to exercise. While the patient was undergoing examination he suffered from attacks characterized by a sudden staring expression, falling backward of his head, slumping of his body and momentary loss of consciousness. These periods were synchronously registered on the electrocardiogram as dropped ventricular beats, auricular impulses maintaining their regular rate and sequence. Atropin was administered intravenously in a $\frac{1}{30}$-grain dose, resulting in

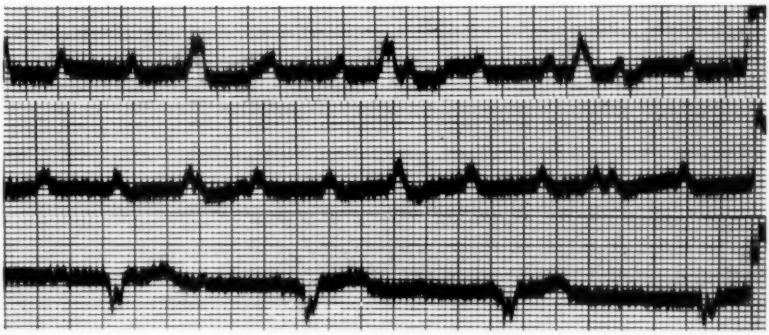

FIG. 1.—Case I.—Initial tracing taken at the time of admission showing complete heart block.

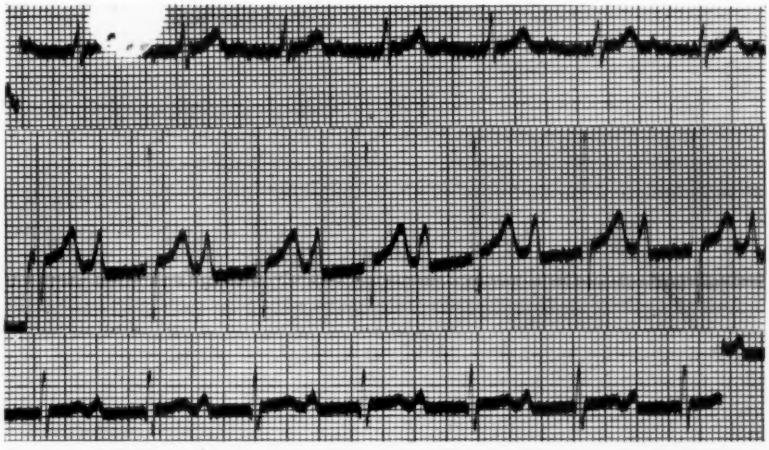

FIG. 2.—Case II. Initial tracing showing large *P* waves and partial heart block.

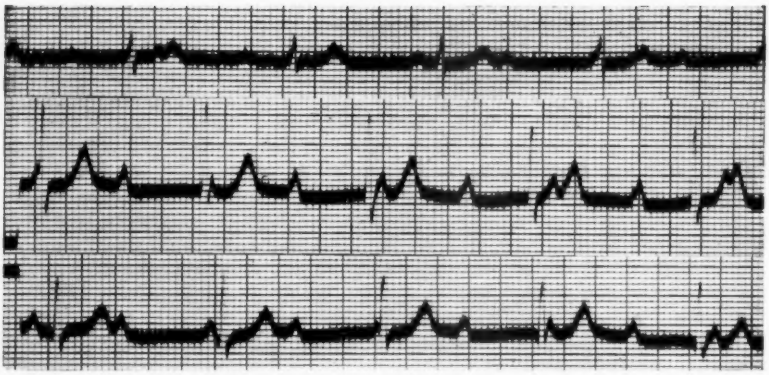

FIG. 3.—Case II. Tracing taken one month after onset of symptoms and showing complete auriculoventricular dissociation.

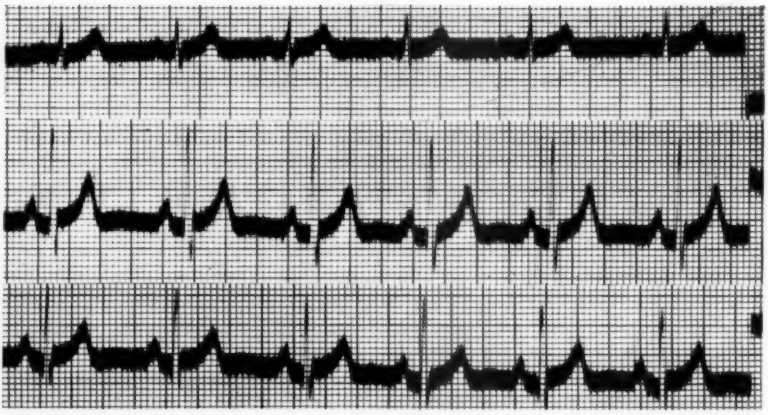

FIG. 4.—Case II. Normal tracing taken after cholecystectomy had been performed.

changes closely resembling those noted by exercise and amyl nitrite, namely, increase in heart rate with no tendency to return to sinus rhythm.

On April 24 the electrocardiogram showed a *P–R* interval of 0.48 second, the *P* wave following immediately after the *S* or *R* wave of the ventricular complex.

The patient had been given potassium iodide for a rather long period, and on May 2 the electrocardiogram showed a *P–R* interval of only 0.2 second.

On May 5 a tracing taken ten minutes after operation showed a *P–R* interval of 0.16 to 0.18 second.

From May 1, 1924, to January, 1925, many electrocardiographical tracings have been taken, all showing normal form (Fig. 4) with no suggestion of the previously noted abnormalities.

Comment. The patient with cardiac gumma presented the usual clinical picture of syphilis of the cardiovascular system, namely, a sudden and unexpected onset with a progressive downward course. We can only surmise that the initiating of her serious difficulty by an apparent Stokes-Adams attack might have also marked the sudden onset of her complete block. She had no similar attacks afterward. The diagnosis of gumma of the septum as a cause for the bundle destruction is conclusively proved by the demonstration in it of the Spirocheta pallida.

The second individual's entire story and progress was unusual. He likewise entered in a state of acute heart failure which was relatively sudden and unexpected in its onset. His heart showed complete auriculoventricular dissociation during the course of our observation, but he progressed to a complete symptomatic recovery with his heart resuming and maintaining normal sinus rhythm.

One might speculate on the relationship between the removal of the infected gall bladder, with the simultaneous recovery and maintenance of normal cardiac mechanism. The "cholecystitic heart" is a well-recognized condition, causing arrhythmia, tachycardia, bradycardia, precordial pain and distress, or even attacks simulating the picture known as angina pectoris. The question here is whether the infected gall bladder caused myocardial changes or strain which was relieved by its removal. This association of myocardial changes and gall-bladder infection has been discussed by Babcock,[3] who has reported several cases in which he attributed myocardial weakness to biliary tract infection.

It is too early to say that this patient has made a permanent recovery. The auriculoventricular bundle having a large reserve conduction capacity may function without showing electrocardiographical changes when only a few strands remain. Under such conditions a slight circulatory change or vagus influence will cause block. This condition of partial bundle destruction may be present

in this man, and the removal of the infected gall bladder by relieving a strain or a toxic effect on the heart might have been sufficient to raise the conduction threshold back to apparently normal function. The potassium iodide which was administered must also be considered in viewing the possible factors that caused the return to normal rhythm and conduction.

The duration of the heart block in this man appears to preclude any possibility of vagus influence being a factor.

Summary. A case of heart block due to gumma of the ventricular septum has been reported.

The diagnosis of gumma has been conclusively proved by the demonstration of the Spirocheta pallida in the ventricular tissues.

The possibility of gall bladder infection as a primary or accessory cause of heart block has been discussed.

A case illustrating the above possibility has been presented in which the heart regained and has maintained normal sinus rhythm since the removal of the infected gall bladder.

We wish to acknowledge our indebtedness to Dr. Frank Hartman for the pathological reports.

BIBLIOGRAPHY.

1. Major, Ralph H.: Arch. of Int. Med., 1923, **31**, 857.
2. Moynihan, Sir Berkeley: (Quoted by H. L. Flint): Brit. Med. Jour., 1920, **2**, 819.
3. Babcock, R. H.: Jour. Am. Med. Assn., 1904, **52**, 1909.

OBSTRUCTIVE JAUNDICE.*

By E. Starr Judd, M.D.,

and

Verne G. Burden, M.D.,

division of surgery, mayo clinic, rochester, minnesota.

Within the last few years, experimental research in the physiology of the biliary apparatus has materially increased our understanding of the basic principles involved in clinical disease of this system. There has been, we believe, a corresponding improvement in diagnosis and treatment. A greater part of the experimental work has been devoted to the consequences of mechanical disturbance of bile flow. While recognizing the great importance of this newer knowledge, we must therefore, be guarded in the application of experimental results in the animal to disease in man. Besides the differences in anatomic structure and physiology, there is the important

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factor of infection, which is the chief cause of disease in man, and is so difficult to reproduce at will in the experimental animal. It is true that the most serious diseases of the biliary tract are those in which the outstanding feature is biliary obstruction. Surgical mortality is practically confined to such cases. There has been, so far as we can determine, very little detailed clinical and laboratory investigation of patients with obstructive jaundice extending over the entire preoperative and postoperative course. The solution of these problems can only be attained by careful comparison of such clinical data with the already known experimental facts. With the idea of stimulating further investigation we report the following case.

A woman, aged forty-four years, came for examination November 29, 1921, because of attacks of abdominal pain. She had been married twenty-one years and had one child. Her present illness had begun one year before, with pain in the right side of the abdomen. A second attack occurred three months later and was followed by persistent soreness over the right side of the abdomen. There were two subsequent attacks about three weeks apart, and a physician was called to relieve the pain. There was no associated fever or vomiting, no jaundice or other symptoms except marked constipation.

The patient was 5 feet, 6 inches high, and weighed 118 pounds. The systolic blood pressure was 144, the diastolic 96. She appeared to be in good health. Abdominal examination was negative except that the right kidney was palpable and mobile. The urine was normal. The hemoglobin was 70 per cent, the leukocytes numbered 8,600. The phenolsulphonephthalein test showed a return of 70 per cent in two hours. Roentgen-ray examinations of the chest, kidneys, ureters, bladder and colon were negative. Electrocardiograms revealed a sinus tachycardia rate of 100. The diagnosis was made of chronic appendicitis, probably associated with cholecystitis, and operation was advised.

December, 9, operation was performed through the upper right rectus incision. The gall bladder was a reddish plum color and filled with stones. It was constricted at the middle, apparently by fibrous tissue. The common duct appeared normal, and stones could not be palpated. The stomach, duodenum, and uterus and adnexa were normal. The right kidney was located normally. The liver was not enlarged but was markedly prolapsed, the lower edge extending below the level of the umbilicus. The gall bladder and appendix were removed and the wound closed without drainage.

The pathologist reported subacute cholecystitis and a contraction in the middle of the gall bladder, and in this contracted portion an adenocarcinoma and squamous-cell epithelioma, grade 2, chole-

lithiasis (multiple stones, the largest 1.5 cm. in diameter), and chronic catarrhal appendicitis (Figs. 1 and 2).

The wound healed by primary union. The patient was dismissed from the hospital on the eleventh day, and returned to her home on the seventeenth day. She returned for examination, September 22, 1924, two years and nine months after the operation. She had been in excellent health until two months before when she had a peculiar uncomfortable sensation high in the epigastrium with a feeling of "drawing." There was no pain. Two weeks later jaundice appeared which became progressively deeper. There was severe pruritus. The urine was dark and the stools clay colored.

The patient now weighed 114 pounds. The systolic blood pressure was 134, the diastolic 88. Jaundice was marked. The liver margin extended below the umbilicus and the surface appeared to be irregular. Urinalysis disclosed a trace of albumin, a large amount of bile, a few hyalin and granular casts, and an occasional pus and red blood cell. The hemoglobin was 67 per cent, the erythrocytes numbered 4,130,000, and the leukocytes 5200. The coagulation time was seven and a half minutes (September 24). Roentgen-ray examinations of the chest and the stomach were negative. Examinations of the stool showed an excess of fat. The patient was sent into the hospital for observation.

September 26, 1924, a test of liver function revealed dye retention, grade 4; serum bilirubin 21.1 mg. for each 100 cc; blood creatinin 1.3 mg. for each 100 cc; and blood uric acid 2.3 mg. for each 100 cc. September 30, the coagulation time was nine and a half minutes, calcium time nine minutes, bleeding time three and a half minutes. These tests were made after the patient had received 4 intravenous injections of 5 cc of 10 per cent calcium chloride. During this time the jaundice had become much deeper.

In view of the previous malignant condition in the gall bladder and the recent onset of painless jaundice it now seemed that a malignant lesion must be causing biliary obstruction. However, the interval of two years and nine months since the previous operation seemed to favor the possibility of a benign stricture of the common duct. The patient was again given a course of calcium chloride intravenously. Fluid intake was increased and quantities of glucose were given by mouth. October 18, biliary obstruction with constant progressive jaundice had existed for eleven weeks. Calcium chloride had been used to improve the coagulation time of the blood. The patient's general condition was excellent. The calcium time was ten minutes and fifteen seconds; the coagulation time eleven minutes. The serum bilirubin was 35.4 mg. for each 100 cc. The bleeding time was three minutes. The salivary urea index was 38 (blood urea 20 mg.).

The risk of operation and the slight hope of cure were explained to the patient and her husband, but they were both anxious to have

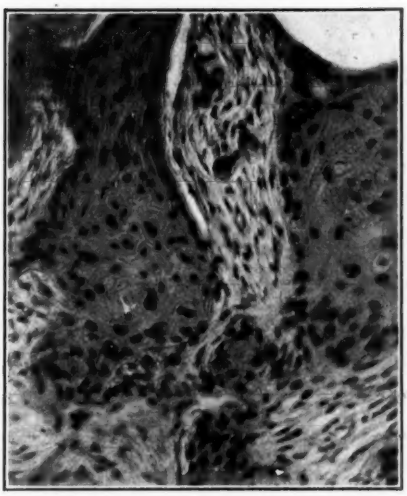

FIG. 1.—Area in gall bladder showing squamous cell epithelioma. (× 200.)

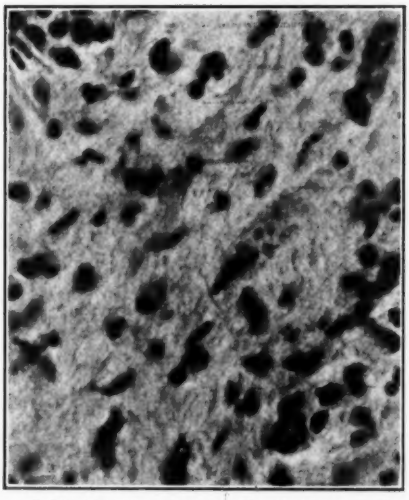

FIG. 2.—Area in gall bladder showing small cell adenocarcinoma. (× 400.)

something done. Therefore, October 20, operation was performed under ether anesthesia. The liver appeared as usual in cases of biliary obstruction. It was enlarged, with rounded edges, mottled, and a dark slate color. Its surface was smooth and uniform. By following the gall bladder notch and keeping close to the liver in dissecting through a mass of scar tissue, the hilus was located. A careful search was made for the common duct but it could not be found. This area was a dense mass of fibrous tissue. Finally a small "bud" was found at the margin of the liver. This was opened and a gush of clear watery fluid, the so called white bile, appeared. A probe was inserted with difficulty along the duct for a short distance into the liver. A passage way distally toward the duodenum could not be found. A small rubber catheter was fastened into this duct which was probably a branch of the main hepatic duct. Several pieces of tissue were excised from the region of the hilus of the liver and examined microscopically; inflammation, marked fibrosis and duct regeneration were found. Two Penrose drains were placed down to the site of operation. The superior surface of the liver, which was widely exposed, was then punctured in many places with a large needle and each time there was a gush of white bile. An ordinary white sponge was placed on the surface of the liver and allowed to remain for drainage. The wound was closed in layers around the drains.

The patient withstood the operation very well, but a transfusion of 500 cc of blood by the citrate method was given as a prophylactic measure.

October 25, bile drainage first appeared.

October 26, bloody drainage appeared; the temperature was 102°, the pulse rate 100.

October 27, the blood urea was 110 mg. for each 100 cc, the creatinin was 2.3 mg. for each 100 cc; the coagulation time eleven minutes, the calcium time ten minutes and fifteen seconds, and the serum bilirubin was 28.6 mg. for each 100 cc.

October 28, the patient had received 3 injections of calcium chloride solution. The coagulation time was ten minutes and forty-five seconds, the calcium time eleven minutes and fifteen seconds.

November 3, the temperature was 100, and the pulse 110. There was considerable edema of the lower limbs, hyperpnea, and complaint of pain in the lower right chest. Examination of the lungs was negative. The drainage of bile varied. The patient was mentally clear and apparently doing well. The blood urea was 240 mg. for each 100 cc, and the creatinin 4.7 mg. for each 100 cc. The output of urine averaged more than 1300 cc daily.

November 5, the blood urea was 259 mg. for each 100 cc; carbon dioxide 20 volumes per cent; and chlorides 570 mg. for each 100 cc.

November 6, the blood urea was 252 mg. for each 100 cc; carbon dioxide 29 volumes per cent, and chlorides 568 mg. for each 100 cc.

November 7, the blood urea was 231 mg. for each 100 cc; carbon dioxide 22 volumes per cent, and chlorides 611 mg. for each 100 cc. Urinalysis revealed only a trace of albumin and a few pus cells. The leukocytes numbered 15,800, the hemoglobin was 40 per cent.

November 8, the blood urea was 215 mg. for each 100 cc; carbon dioxide 28 volumes per cent, and chlorides 571 mg. for each 100 cc. There was good drainage of bile.

November 10, the blood urea was 251 mg. for each 100 cc, and chlorides 637 mg. for each 100 cc.

November 11, the blood urea was 189 mg. for each 100 cc; carbon dioxide 32 volumes per cent, and chlorides 624 mg. for each 100 cc.

November 12, the blood urea was 144 mg. for each 100 cc; carbon dioxide 26 volumes per cent, and chlorides 619 mg. for each 100 cc.

November 13, the blood urea was 117 mg. for each 100 cc, and the chlorides 616 mg. for each 100 cc. The patient was given, intravenously, 1000 cc of 10 per cent glucose and 4 per cent sodium bicarbonate at 5.30 P.M., after which the blood urea was 253 mg. for each 100 cc; the carbon dioxide 24 volumes per cent; the chlorides 609 mg. for each 100 cc, and the serum bilirubin 4.2 mg. for each 100 cc. For several days there had been bile in the stools and diminishing jaundice. Removal of the gauze drain was started on the twelfth day and completed on the sixteenth. The Penrose and Robson drains had been removed.*

November 14, an intravenous injection of 500 cc of 10 per cent glucose and 4 per cent sodium bicarbonate was given. The urinalysis revealed a trace of albumin, bile, urobilin, no casts and an occasional pus cell.

November 15, an intravenous injection of 250 cc of 10 per cent glucose and 4 per cent sodium bicarbonate was given. The blood urea was 92 mg. for each 100 cc; carbon dioxide 56 volumes per cent, and chlorides 570 mg. for each 100 cc.

November 17, the blood urea was 70 mg. for each 100 cc; carbon dioxide 82 volumes per cent, and the chlorides 506 mg. for each 100 cc.

November 18, the blood urea was 49 mg. for each 100 cc; carbon dioxide 76 volumes per cent, and the chlorides 519 mg. for each 100 cc. The patient's general condition was so much improved that

* It may be noted that on November 3 and 5, the laboratory reports indicated a condition of renal insufficiency and acidosis. A solution of 375 cc of 4 per cent sodium bicarbonate and 20 per cent glucose was given intravenously. There was a responsive improvement in the acidosis, as shown by the increased carbon dioxide combining power of the blood. During the succeeding seven days glucose solution was given intravenously almost daily, sometimes in combination with sodium bicarbonate or sodium chloride. The only reaction occurred November 13. The patient's condition was markedly improved. It is of interest to contrast the daily laboratory reports of the relative values of blood urea, carbon dioxide, and chlorides with the findings in the acute toxemia of intestinal stasis. The blood urea was high, the blood chlorides were normal, and there was acidosis. With the toxemia of stasis the blood urea is high, the plasma chlorides are diminished and there is an increase in the alkali reserve.[5]

she was allowed to be up in a wheel chair. Bile drainage continued but the stools were natural in color. Her appetite was good; her only complaint was weakness.

November 20, the blood urea was 48 mg. for each 100 cc; carbon dioxide 65 volumes per cent, and the chlorides 540 mg. for each 100 cc.

November 21, the patient complained of pain in the right lower chest, which was worse on deep inspiration. The temperature was 101°. There was no drainage of bile to the outside for twenty-four hours.

November 22, the patient was much improved.

November 24, the blood urea was 36 mg. for each 100 cc; carbon dioxide 70 volumes per cent, and the chlorides 579 mg. for each 100 cc. The output of urine averaged about 1000 cc daily. There was free drainage of bile. The patient was walking with assistance. During convalescence the temperature remained around 99.5°, but several times took a sharp rise to 102.°

December 2, the blood urea was 23 mg. for each 100 cc; the carbon dioxide 52 volumes per cent, and chlorides 621 mg. for each 100 cc.

December 9, the patient was dismissed from the hospital. The stools were normal in color. The jaundice, judging from the appearance of the sclera, had entirely disappeared. The wound continued to drain a small quantity of bile and required a change of dressing daily. The entire right hypochondrium was filled by the liver which extended to the level of the umbilicus.

The patient was kept under observation at a convalescent home. While there she had several attacks of pain in the right hypochondrium which were promptly relieved by resumption of drainage from the biliary fistula. She gained in weight and strength and was allowed to go home January 6, 1925. At that time there was no trace of jaundice. A fistula was discharging bile but there was also bile in the stools.

Discussion. The value of the intravenous administration of calcium chloride in the preoperative preparation of jaundiced patients is well known. Walters has shown that by this method the prolonged coagulation time of the blood is brought within the limits of safety. Our practice is to give, on successive days, 3 intravenous injections of 5 cc of a 10 per cent solution of calcium chloride. If improvement is not satisfactory these injections are repeated after an interval of several days. There is no untoward effect on renal function following such dosage.[1] The patient seems to improve independently of the reduced coagulation time of the blood. This is borne out by the experimental results of King, Bigelow, and Pearce in cases of obstructive jaundice. They found an increase in the calcium content of the blood and kidneys and suggested that the calcium is bound to the bile pigments to neutralize their toxic effects, and is probably not available for the clotting of blood. There

is also a loss of calcium in the feces. The mobilization and expenditure of calcium probably occur at the expense of bone. It therefore seems probable that the administration of calcium to jaundiced patients not only improves the coagulation of the blood but helps to neutralize the toxic effects of bile in the blood. Although our patient had been deeply jaundiced for eleven weeks, there was no oozing of blood after the operation. Another point of interest in our case is that nearly three years after the operation there was no local evidence of recurrence of the malignant condition, either grossly or in microscopic sections removed from the region of the gall bladder. It is possible that in early carcinoma of the gall bladder, usually an accidental finding with gall stones, cholecystectomy will effect a cure, although this lesion provides some of the darkest pages in the dark chapters on carcinoma.

There are several features in our case that seem to defy explanation: The complete absence of a common duct. There had been an uncomplicated cholecystectomy for stones at which time the common duct appeared to be normal and was not opened. The wound which was closed without drainage healed by primary union and the patient was dismissed from the hospital on the eleventh day. She remained entirely well for more than two and a half years when painless jaundice developed. The process might have been an obliterative cholangitis analogous to a similar condition often seen in the appendix. We cannot explain the passage of bile into the intestine unless by a pocket connecting the bile duct with the duodenum. At the time of operation there was no passage way for the bile to the intestine, and none was made.

The liver in cases of obstructive jaundice has been the subject of much study. In the dog, where anatomic arrangement permits ducts draining separate portions to be occluded, it has been shown that obstruction of bile from a portion of the liver leads to complete parenchymal atrophy in that part. A very small part of the liver is sufficient to carry on the work of the whole.[3] However, when the common duct is occluded the entire liver is affected, and the patient dies when demonstrable hepatic changes are only slight. Our case afforded a clinical example of the "white system" described by Rous and McMaster. When the stump of the hepatic duct was opened there was a gush of white bile under pressure. They give a more accurate description which fits this instance under the term *hydrohepatosis*.[4] In this condition, the intrahepatic bile ducts are distended with a thin colorless fluid which is devoid of bile salts or pigment, and which is a secretion of the ducts themselves.[7] In many respects it is analogous to hydronephrosis. In this case and in many similar cases we have pierced the upper surface of the liver deeply in many places with a large needle. This is followed by free oozing of a thin colorless fluid from the puncture holes. A continu-

ous slow decompression of the liver results. The bleeding is not troublesome.

Glucose is of great value for these very sick and jaundiced patients. According to Mann it is almost a specific for hepatic insufficiency. It may be given intravenously in 10 per cent solution. Blood transfusion is also a helpful, although there has been no actual loss of blood.

While the liver has a wide margin of safety, its functional capacity cannot be estimated accurately in cases of obstructive jaundice. It is common knowledge that operation for relief of biliary obstruction is often followed by variable and uncertain events, particularly when the ducts contain white bile. In some cases there is good drainage of normal colored bile very soon after operation; in some, pigment may not appear for several days, or having once appeared will stop, and in others, bile fails to appear in spite of unobstructed drainage, and the patient dies from so called cholemia. Such events cannot be forecast at operation, and there is no fixed relation to the duration or degree of jaundice. The underlying factor is probably the functional capacity of the liver. Rous and McMaster have suggested that the rate of the disappearance of jaundice after relief from biliary obstruction might furnish an index of hepatic function. In our case the intrahepatic ducts were filled with white bile, and bile pigment did not appear in the drainage until the sixth day after operation. The serum bilirubin, which was 35.4 mg. for each 100 cc two days before operation, dropped to 28.6 on the eighth day after operation, and twenty-five days afterward it was 4.2 mg. for each 100 cc.

One of the chief symptoms of which jaundiced patients complain is an intolerable pruritus, which is a constant menace to rest. This symptom often precedes the definite appearance of jaundice. The ordinary methods of relief are futile. The most marked benefit we have seen has followed the use of diathermy, but the relief is temporary and is not so easily obtained by subsequent treatments. We noted, in many instances, that the pruritus completely and promptly disappeared following the establishment of free drainage of bile after biliary obstruction long before a reasonable time for the elimination of retained bile salts. That the itching is not caused by the increased bile pigment in the blood is demonstrated by the fact that many patients, when relieved from their obstruction, may nevertheless remain jaundiced for several weeks, but they do not have pruritus, and with hemolytic jaundice, itching does not occur.

Summary. A case of postoperative obstructive jaundice is reported. Significant laboratory studies were made of the blood before and after operation. There was no evidence of recurrence more than two and a half years after removal of a cancer of the gall bladder. A method is described of decompression of the liver by multiple needle punctures into the hepatic parenchyma.

BIBLIOGRAPHY.

1. Bowler, J. P. and Walters, Waltman: The Effect of the Intravenous Injection of Calcium Chloride on the Kidney, Jour. Am. Med. Assn., 1924, **83**, 1232–1236.

2. King, J. H., Bigelow, J. E., and Pearce, L.: Experimental Obstructive Jaundice Jour. Exper. Med., 1911, **14**, 159–177.

3. McMaster, P. D. and Rous, P.: The Biliary Obstruction Required to Produce Jaundice, Jour. Exper. Med., 1921, **33**, 731–750.

4. McMaster, P. D. and Rous, P.: Hydrohepatosis, a Condition Analogous to Hydronephrosis, Proc. Nat. Acad. Sci., Baltimore, 1923, **9**, 19–21.

5. McVicar, C. S.: A Discussion of the Clinical and Laboratory Findings in Certain Cases of Obstruction in the Upper Gastro-intestinal Tract (The Rôle of Blood Chemistry in Diagnosis, Prognosis and Treatment of this Condition), Am. Jour. Med. Sci., 1925, **169**, 224–235.

6. Mann, F. C. and Magath, T. B.: Studies on the Physiology of the Liver, Am. Jour. Physiol., 1921, **55**, 285.

7. Rous, P., and McMaster, P. D.: Physiological Causes for the Varied Character of Stasis Bile, Jour. Exper. Med., 1921, **34**, 75–95.

REVIEWS.

A TEXTBOOK OF PRACTICAL THERAPEUTICS. By HOBART AMORY HARE, B.Sc., M.D., LL.D., Professor of Therapeutics, Materia Medica and Diagnosis in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital; one-time Clinical Professor of Diseases of Children in the University of Pennsylvania; one-time Commander, M.C., U.S.N.R.F. Nineteenth edition. Pp. 1061; 144 engravings and 8 plates. Philadelphia and New York: Lea & Febiger, 1925.

HARE'S *Practical Therapeutics* needs no eulogy and adverse criticism of it is almost impossible. It is a finished product and the profession's approval of it is evidenced by the nineteen editions. This last one particularly will make its appeal because of the numerous additions to the text. Among these may be mentioned sulpharsphenamin, insulin and the newer hypnotics. Even certain drugs, such as dial and medinal, which have not as yet been accepted by the Council on Pharmacy and Chemistry of the American Medical Association, are included. It is only fair perhaps, in spite of what has been said, to point out that some of the illustrations are somewhat antiquated and that there is an error on page 132 where it is stated that the spinal fluid should be withdrawn until the manometer shows the pressure to be about 30 mm. of "mercury."

T. M.

CHEMISTRY AND CHEMICAL URINALYSIS FOR NURSES. By HAROLD L. AMOSS, M.D. Third edition. Pp. 241. Philadelphia: Lea & Febiger, 1925. Price, $2.25.

CHEMISTRY, as taught in schools of nursing, due to the limited time, must of necessity cover only a few general principles which may be applied to nursing. The writer has endeavored to adapt his book to the needs of the student nurse; however, the nursing references are not as numerous as might be desired. Throughout the text important words and statements are in italics and the divisions of each chapter are readily seen in bold black type. Each chapter is concluded by a brief summary which is concise and should serve as an excellent review. The text as a whole is interestingly written, the arrangement of subject material is good, and it should be an excellent text for the teacher of nurses or the student who wishes to continue her study of chemistry.

E. K.

THE ADVANCE OF ORTHOPEDIC SURGERY. By A. H. TUBBY, C.B., C.B.E., M.S. (LOND.), F.R.C.S. (ENG.), F.S.A. COL. R.A.M.C. (retired), and formerly Consulting Surgeon, Mediterranean and Egyptian Expeditionary Forces; Consulting Surgeon to the Westminster Royal National Orthopedic, Evelina and Christ's Hospitals; Member of the International Society of Surgery, of the Société Française de Chirurgie, of the Société de Chirurgie de Paris, and of the British Orthopedic Society; Corresponding Member of the American Orthopedic Association. Reprinted from the *Clinical Journal*. Pp. 144; 31 illustrations. London: H. K. Lewis & Co., Ltd., 1924.

THE author offers six articles written for *The Clinical Journal* and republished in book form which abstract the advances made in Orthopedic Surgery in the last twelve years. The roentgen-ray diagnosis of bone and joint conditions is covered most completely. The congenital and growth deformities are well described and well illustrated, and given in very practical form. The dangers of static and postural conditions are well emphasized. The infantile and spastic paralysis with discussion of etiological diagnosis and treatment are most comprehensively covered. The problem of the care and cure of cripples in large communities is thoroughly discussed. D. W.

ON THE BREAST. By DUNCAN C. L. FITZWILLIAMS, St. Mary's Hospital, Paddington. Pp. 440; numerous illustrations. St. Louis: C. V. Mosby Company, 1925.

IN this, the American edition of the English work by the abovementioned author, attempt has been made to furnish the surgeon, the student and the general practitioner with a condensed and adequate detailed account of the diseases of the breast and the methods of treatment. It is well stated that the majority of the works on breast are either too exhaustive for a busy man to wade through or too elementary to be of any use in connection with a case needing reference. The author furnishes the reader with clear-cut clinical pictures that are of sufficient fulness of description to be of reference value. Scattered throughout the text are numerous case histories and references which tend to fix in the reader's mind the essential embryologic, pathologic and anatomic features concerned with the condition under discussion. The book is profusely illustrated by pen and ink drawings, the majority of which are original. My one criticism of the illustrations is that possibly a little too much emphasis is placed upon the monstrosities of pathology. The book can be well recommended for student perusal. E. E.

PHYSICAL CHEMISTRY FOR STUDENTS OF MEDICINE. By ALEXANDER FINDLAY, M.A., D.Sc., F.I.C., Professor of Chemistry, University of Aberdeen. Pp. 227. London: Longmans, Green and Company, 1924.

PROFESSOR FINDLAY, a recognized authority in physical chemistry, has contributed an elementary work based on the course in medical physical chemistry as given at the University of Aberdeen. The theoretical treatment is expounded in the author's usual explicit style, and is well illustrated by examples selected from medical and biological literature. The rapid growth of this subject has probably precluded the introduction of some more recent applications, though as a guide to these advances, this book should be welcomed by teachers, investigators and clinicians alike. B. O.

GONORRHEA. By DAVID THOMSON, Honorary Pathologist and Director of the "Pickett-Thomson" Research Laboratory, St. Paul's Hospital, London. Pp. 519; 22 illustrations and 21 plates, 2 in colors. London: Henry Frowde, Hodder & Stoughton, 1923.

THE monograph under consideration is very comprehensive in its scope, dealing with every aspect of gonorrhea. The author has done much research in this field and the results of his investigations concerning the complement fixation test and vaccine therapy are given at length. The publishers can feel proud of the volume, as it is most attractive in appearance, contains beautiful photomicrographs and colored plates, and the many bibliographies in various parts of the work are of real value. The section devoted to the female organs is not as complete as the remainder of the book; for example, stricture of the female urethra is not mentioned and pelvic inflammatory disease is very superficially, and to American minds, very poorly presented. As monographs appeal most strongly to specialists, this volume should be of interest to the urologist, serologist and bacteriologist. F. B.

GYNECOLOGY WITH OBSTETRICS. By JOHN S. FAIRBAIRN, Obstetric Physician, St. Thomas's Hospital, London. Pp. 769; 129 illustrations and 5 plates. London: Oxford University Press, 1924.

THIS book is intended for students and is of sufficient scope to be of value to them. In the beginning of the book is a rather

interesting historical prologue, although it will probably appeal very little to the average student. In the treatment of the subjects announced this book goes into somewhat more detail than the average handbook or manual, although it does not compete with the standard large textbook. On the whole, the section on obstetrics is better presented than the part devoted to gynecology, and the omission of any reference to Rubin's tubal inflation test and Sampson's interesting work with "chocolate" cysts of the ovary can hardly escape the notice of an American reviewer. Some of the illustrations are very satisfactory, but many of them are simple line drawings. Aside from being useful as a student's handbook, it might be helpful as a quick reference to general practitioners. F.B.

A Laboratory Manual of Physiological Chemistry. By E. W. Rockwood and P. R. Rockwood, Department of Chemistry and Toxicology, University of Iowa and the Mayo Foundation. Fifth edition. Pp. 406; 43 illustrations. Philadelphia: F. A. Davis Company, 1924.

This volume is a very good laboratory textbook for a rather extensive course in physiological chemistry, designed especially for medical students. The material is up to date and arranged in a very systematic manner, beginning with the foodstuffs and ending with the excretion of the urine. The chapter on Acid-base Equilibrium is brief and somewhat incomplete, but probably sufficient for medical students. The methods for blood and urine constituents are well chosen, complete and comprehensive. The arrangement of the book is not as inviting as some similar manuals, but the experiments are in general better selected.

W. K.

Operative Surgery. By J. Shelton Horsley, M.D., F.A.C.S., St. Elizabeth's Hospital, Richmond, Va. Pp. 784; 666 illustrations. St. Louis: C. V. Mosby Company, 1925.

The greatest change in the second edition of this book is in the addition of a chapter on The Principles of Operations for Malignant Growths, in which some of the recent views of cancer are stated and their bearings upon operation for the cure of malignant tumor is noted. Among the interesting new operations described in this edition are the following: The lymphaticostomy of Costain, the operation of Stookey for innervating paralyzed muscles, the pylorectomy of Finney, the pulmonary lobectomy of Graham, the valvotomy of Cutler for mitral stenosis, the operation for angina

pectoris, the chordotomy of Frazier and the intestinal resection of Kerr. The operations of Crile for partial lobectomy of the thyroid and for ligation of the superior thyroid arteries are fully described, as well as gastroenterostomy and gastrectomy. The book is nicely gotten up, well written, cleverly illustrated and represents the last word in operative surgery. E. E.

DISEASES OF THE RECTUM. By MARTIN L. BODKIN, M.D., F.A.C.S. Pp. 487; 111 illustrations. New York: E. B. Treat & Co., 1925.

THIS, the second edition of the work, has added chapters on Irrigation of the Colon, Superficial Diseases of the Anal Region and Relation of the Intestinal Flora to the Simple Catarrhal Diseases of the Colon. The older material on operations and treatment of malignant diseases has received careful revision. A special chapter has been added on Perianal Diseases, and a great deal of attention given to the bacteriology causing the different types of intestinal mucosa diseases. Attention is further given to the relation of rectal diseases to gynecology. The book is at once a practical and comprehensive treatise on this very important subject. It is well illustrated by good illustrations, printed on excellent paper and written in an easy, pleasing style.

E. E.

MEDICINE. AN HISTORICAL OUTLINE. By M. G. SEELIG, M.D., Professor of Clinical Surgery in the Washington University School of Medicine. Pp. 207; 48 plates. Baltimore: Williams and Wilkins Company, 1925.

UNDERGRADUATE acquaintance with even the high lights of medical history is unfortunately becoming more or more imperfect in these days of crowded curricula, when the unfortunate student must not only have acquired certain premedical scientific requisites, but must also squeeze into his already inadequate four years the steadily increasing bulk of medical and borderline knowledge. Not only must the clinical and preclinical subjects be taught by the necessarily time consuming "laboratory method" of instruction; but new instrumental methods and new subjects such as biophysics and physical chemistry are constantly crowding for recognition. Small wonder then that such apparent unessentials as the past history of medical art, teeming as it is with foolish errors and superstition, is neglected. Let the dead bury its dead!

But is not perhaps medical education like Macbeth's "vaulting

ambition which overleaps itself and falls on the other?" Is not the present method in some ways impractical and inefficient? Surely complete ignorance on the part of the student, say, of the man, time and circumstances connected with the discovery of the tubercle bacillus, must handicap his ability to deal with tuberculosis, necessitate more time in teaching him its "practical" phases and leave him more defenceless against the propagator of future errors. As Charles Singer maintains and demonstrates in London, sensible lectures on medical history not only provide the hearers with a better perspective of their subject, but actually save curricular time by offering a common foundation and often preventing repetition.

Anyone sympathizing with this point of view will welcome Major Seelig's book. Presenting the high lights of medicine in a somewhat breezy and attractive manner, it is well calculated to "tempt the student to dip into medical history." With Garrison's well known history and our interesting Annals of Medical History easily available, there is little likelihood of the awakened interest being later frightened away from the subject by the bulk of ponderous authorities. The reviewer thoroughly agrees with the remarks of Dr. Garrison in the Foreword that "the lectures are fresh, informing, brief and to the point . . . while the author's racy idiom, the stimulus of his enthusiasm and his slant on various matters are his very own." The St. Louis schools of medicine are to be congratulated on having the originals of these lectures available for their senior students. May the example prove contagious.!

E. K.

Cosmetic Surgery—The Correction of Featural Imperfections. By Charles Conrad Miller. Pp. 263; 141 illustrations. Philadelphia: F. A. Davis Company, 1924.

The object of this book is to be a guide to the surgeon in the correction of cosmetic defects of the face. The author describes numerous operations for the correction of folds, tags and wrinkles about the eyes, for the lifting of the face, for altering the palpebral interval, for the correction of double chin, for the softening of nasolabial lines, for the eradication of scowl lines, the formation of dimples, and other similar procedures. When he says that "all operations described in the book—can therefore be performed in the office quite as well as in a hospital operating room" he is minimizing a branch of surgery which is technical and demands considerable ingenuity in its performance. While a few of the author's operations have something to commend them, such as that for partial stenosis of the nose or for the correction of outstanding ears, there is considerable doubt in the reviewer's mind as to the end results obtained from most of the procedures suggested. Among these

are the operation for double chin and that for the removal of nasal bumps. The majority of the operations are inadequately described, the illustrations are not anatomical and the author has included no photographs of end results of his own cases. The operations are made to appear too simple and the reviewer fears that the book may do actual harm in leading the inexperienced surgeon to attempt technically difficult procedures without forewarning as to the difficulties which he will encounter.

There is considerable question as to the ethics involved in performing operations of this type. The author realized the possibility of criticism when he said, "in the face of possible strictures from the best in the profession, the writer offers these pages to those who may be interested." I. R.

HEREDITY IN NERVOUS AND MENTAL DISEASE. An investigation by The Association for Research in Nervous and Mental Disease. Pp. 332; 48 illustrations. New York: Paul B. Hoeber, Inc., 1925.

A MONOGRAPH consisting of a series of well-prepared articles on the various phases of heredity in nervous and mental disease. Five main subdivisions are considered: I. The role of the cell and the chromosomes and the significance of exogenous and endogenous factors in heredity. II. The parts of the central nervous system which tend to exhibit morbid recessive or dominant characters. III. Pathological aspects: in the nervous system, in the extraneural systems and experimental degeneracy. IV. Heredity in the psychoses. V. Heredity in literature.

The book is well edited, the discussion is lively and serves to bring out the salient points, and the illustrations are excellent. Certain articles deserve more than passing mention: "The Modern and Technical Study of Heredity" by Charles L. Dana; "The Cellular Basis of Inheritance" by Charles W. Metz, with a discussion of 11 pages; "Experimental Production of Degeneracy" by Charles R. Stockard and Albert M. Barrett's contribution on "The Heredity and Familial Factors in the Development of the Psychoses." N. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE.

ROGER S. MORRIS, M.D.,

TAYLOR PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI.

AND

JOHN H. MUSSER, M.D.,

PROFESSOR OF MEDICINE, TULANE UNIVERSITY OF LOUISIANA, NEW ORLEANS.

Studies on the Pathological Histology of Experimental Carbon Tetrachloride Poisoning.—The large number of patients, over 1,000,000, who have been treated for hookworm and other parasitic worms with carbon tetrachloride, testify to the value of this preparation as an anthelmintic. It is comparatively pleasant to take, or at least it is much less disagreeable than other anthelmintics and it has been found relatively safe. However, the fact that several deaths have occurred following the administration of CCl_4 led GARDNER and others (*Bull. Johns Hopkins Hosp.*, 1925, **36**, 107), at the request of the International Health Board, to undertake a study of the toxicity, pharmacology and pathological changes that take place following its ingestion. For the purposes of the investigation 240 dogs were employed; chemically pure CCl_4 was secured; the drug was given by stomach tube, subcutaneously, intraperitoneally, by inhalation, by rectum and intravenously; and various size doses were given per kilo of body weight. The drug was also given in conjunction with cream and with alcohol. The authors accentuate in the report that the only lesion worthy of note produced by carbon tetrachloride is a central necrosis of the liver. This is observed as early as twelve hours after oral administration and may be produced by an oral dose of the drug equivalent to 0.5 cc per kilo of body weight. Healing of the liver lesion begins three to four days after the oral administration of the drug and is not completed in five weeks. In addition to the result that the authors stress in their paper, there are two or three other points upon which it is interesting to

speculate. They note that puppies are more susceptible to the drug than adult dogs and that rabbits are more susceptible than dogs, probably because there is no cathartic action from the drug in rabbits as there is in man and dog. Among the 12 puppies that were given equivalent dosage for weight, 6 died and of the 6 who died 3 had masses of dead roundworms in their small intestine. These latter results suggest the advisability of using the drug with extreme caution when administered to children, not only because the liver of the young seems to be more susceptible, but also because of the possibility that in children roundworms may be present which might cause a partial or incomplete obstruction of the lumen of the intestine when killed by the action of the drug and a consequent slower elimination than when peristaltic action is unimpeded. Such a sequence of events apparently occurred in a fatal case recently seen following administration of CCl_4 and as yet unreported. The masses of dead worms in the intestine of the child were sufficiently obstructive apparently to cause a retention of the drug which killed the child by its action on the liver cells, as confirmed by autopsy a few hours after ingestion. The studies of the authors would make it seem proper to utter a word of caution to those who would administer CCl_4 to children and more particularly to children who might have an infestation of the large worm parasites as well as hookworms.

Contributions to the Pathology of Experimental Virus Encephalitis. III Varieties and Properties of the Herpes Virus.—SIMON FLEXNER and H. L. AMOSS (*Jour. Exper. Med.*, 1925, **41**, 357) in the third paper of the series dealing with experimental virus encephalitis, recount their experiences with, and studies of, some strains of the herpes virus which are much less likely to produce encephalitis in the rabbit than the two highly virulent strains, previously reported upon. With these mild strains the authors found that their action was largely confined to the point of inoculation. These strains would produce a local keratoconjunctivitis if injected into the eye or a dermatitis when given subcutaneously and recovery was the rule without invasion of the central nervous system. Recovery is followed by an immunity to the virulent strains of herpes virus. They find that long glycerolation will frequently reduce the virus so that it is impossible to secure effective extracranial inoculation. The detection of herpes virus in the buccal secretions of healthy persons by rabbit experiment is unsuccessful and in the case of sufferers from labial herpes it is extremely difficult. The detection of the virus in cerebrospinal fluid is also attended with great difficulty, while the escape of the herpes virus through the urine is for the first time demonstrated by finding it in the urine in several rabbits. Another point brought out in the authors' paper is that, in spite of the known fact that one attack of virus infection affords almost complete immunity, it has not been definitely proven that the blood serum can neutralize the virus *in vitro*. Neutralizing substances occur in the blood of animals recovered from infection with the herpes and allied virus, yet are usually absent from human serum. "The conspicuous absence of the substance from the convalescent serum of cases of epidemic encephalitis argues against that disease being etiologically connected with one of the allied viruses." The series of papers close with a comparison of the clinical manifestations of the disease as it appears in man and rabbit.

The Sugar Content of the Cerebrospinal Fluid and its Relation to the Blood Sugar.—GOODWIN and SHELLEY (*Arch. Int. Med.*, 1925, **35**, 242) found the cerebrospinal sugar content to be least fluctuant before breakfast, just as with the blood sugar. The cerebrospinal sugar exhibits much the same variations throughout the day (and in many diseases) as does blood sugar, although the peak rises following meals are not seen. The sugar in cerebrospinal fluid usually falls between 45 and 65 per cent of that in the blood regardless of the time of the determination. In diabetes, for instance, both fluids show roughly similar percentage sugar increases. It is obvious that sugar determinations on the cerebrospinal fluid alone at any time would be of little value. Encephalitis cases usually show a higher sugar content of the cerebrospinal fluid in relation to the blood sugar content, while in early cerebrospinal syphilis the opposite is found. Low actual and relative figures are also obtained in meningitis, whether tuberculous, staphylococcic or meningococcic in origin.

All-day-blood-sugar Curves in Non-diabetic Individuals and in Diabetic Patients with and without Insulin.—LEON JONAS, T. GRIER MILLER and IDA TELLER (*Arch. Int. Med.*, 1925, **35**, 289) present a very valuable study of the all-day-blood-sugar variations, showing maximum rises shortly after the morning and evening meals much more frequently than after the noon day one. This occurs in most diabetic patients with much greater regularity than in normal individuals. Curiously enough, the morning rise is usually greater than the evening one, and reaches its peak about one hour after breakfast. For mild cases of diabetes on a maintenance diet divided evenly between the three meals, a single dose of insulin administered a half hour before breakfast sufficiently controls the blood sugar for the whole day. More severe cases require an additional dose, somewhat smaller, a half hour before the evening meal. If the morning fasting level of blood sugar is too high with the two doses, a third one is most effective given about midnight. This work brings out very nicely the value of proper timing of the insulin injections to yield a maximum control of the sugar metabolism.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE MEDICAL SCHOOL AND ASSOCIATE PROFESSOR OF SURGERY IN THE SCHOOL FOR GRADUATES IN MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

The Nomenclature Used by the Registry of Bone Sarcoma.—CODMAN (*Am. Jour. Roentgenol.*, 1925, **12**, 105) states that for all intents and purposes, the person who presents himself with a bone tumor, which

is not inflammatory or metastatic, may be told that he has one of five tumors: Periosteal fibrosarcoma, prognosis fair with complete excision; benign osteogenic tumor, prognosis excellent with radical excision; osteogenic sarcoma, prognosis bad no matter what its treatment, although a few recoveries following amputation are on record; benign giant-cell tumor, prognosis good under almost any treatment, except bad surgery; Ewing's tumor, prognosis good for immediate reduction under roentgen radiation, but eventually bad; myeloma, certainly and slowly bad but probably retarded by radiation. All these types have their definite roentgen-ray criteria, and all these types have pretty definite microscopic and clinical characteristics. Cases of osteogenic sarcoma die pretty quickly whether they are fibro, chondro, osteo, round- or spindle-cell, and Ewing's tumor is no worse for being called multiple, diffuse, central, alveolar, perithelial or invasive.

The Cholesterol Content of the Blood in Relation to Genitourinary Sepsis.—MacAdam and Shiskin (*Brit. Jour. Surg.*, 1925, **12**, 435) say that in only about 50 per cent of the patients with a low cholesterol value, who subsequently died of pyelonephritis, did clinical opinion of the general condition of the patient contraindicate operation. In many instances, therefore, no certain information as to the resistance of the patient to postoperative spread of sepsis is afforded by considering the patient's clinical condition alone. The authors suggest that a low "blood cholesterol" in a case of acute or chronic retention due to prostatic enlargement is significant of a low capacity for antibody formation and points to the case being a bad operative risk as regards prostatectomy. Genitourinary sepsis with the risk of ascending infection is of more serious prognostic import than nitrogen retention from defective renal function. A high blood urea alone is not necessarily serious to ultimate prognosis—on the other hand, the combination of a high blood urea and a low cholesterol content is of very serious prognosis and points to an undoubtedly bad surgical issue.

The Surgical Treatment of Cleft Palate—Dowd (*Ann. Surg.*, 1925, **81**, 573) believes that these children should have their defects repaired by the time speech is established. The operation on the lip should be done at the earliest practicable time. In many instances correction of the alveolar process and of the nasal deformity may be begun at the same time as the lip operation. The hard palate should ordinarily be repaired a few months after the primary operation on the lip and alveolar process. Metal plates and iodoform gauze packing are helpful in securing a good result. Usually the operation on soft palate should not be done until the hard palate has suitably united. The soft palate should be protected from traumatism and no tissues should be removed, excepting the small margin of the cleft. This repair should be accomplished at a single operation. It is the most delicate structure with which we have to deal. It should be conserved to the fullest possible degree. Speech instruction should be begun early and carried out persistently and carefully under skilful directions.

An Operation for Unreduced Posterior Dislocation of the Elbow.—Speed (*South. Med. Jour.*, 1925, **18**, 193) says that the operation is suit-

able in all uncomplicated posterior dislocations of the elbow, which have remained out a sufficient length of time to prevent closed reduction without undue trauma to the joint. After the second or third week closed reductions are generally not satisfactory. In the doubtful cases much less damage will be done and a much better functional result obtained by an open reduction. In cases complicated by extensive fractures and bony ankylosis an arthroplasty of the elbow offers the only hope of a movable joint. The author has employed the operation in a number of cases with most gratifying results. The amount of function depends upon the length of time the dislocation has existed and whether the case is an adult or child. Four of the cases were in children, three of whom had been injured between eight and twelve weeks. All of these obtained practically normal motion and a perfect functional result. One that had been dislocated eight months had about 60 per cent normal motion after six months. However, sufficient function had been reëstablished to induce normal growth and development. One adult of ten weeks' duration, with the elbow in full extension and no motion in any direction, regained a complete range of supination and pronation and about 40 per cent flexion. A second adult with a dislocation of only six weeks' duration was making excellent progress at discharge. The technic and postoperative care are given in full in the article.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

Factors Involved in the Acidity of Stools of Infants.—BROWN and TISDALL (*New York State Med. Jour.*, 1925, **25**, 152) studied 1300 specimens for the determination of the pH of infants' stools. The pH of stools from normal, newborn breast-fed infants was found to be singularly constant, varying from 4.7 to 5.1. The acidity of stools from artificially fed infants was found to vary from pH 4.6 to somewhat more alkaline than pH 8.3. An acidity as great as pH 4.6 was encountered in artificially fed infants only in severe diarrheal conditions. Infants fed on butter soup generally had stools with an acidity of about pH 6.0. Infants fed on protein milk, cows' milk dilutions with added carbohydrate generally had stools more alkaline than pH 7.0 whole soured milk, with added carbohydrates up to a total content of 20 per cent, generally produced strongly alkaline stools. No difference was consistently observed in the acidity of the stool, whether the added carbohydrate was in the form of corn syrup, dextrimaltose or cane sugar. In this investigation the effect produced by other sugars was

not determined. The degree of acidity of the stools was generally increased in the presence of parenteral infection. The factors which influence follow. The acidity apparently depends on the ration in the intestinal zone of fermentation, of the carbohydrate on one hand to the protein and the base on the other. The amount of carbohydrate in the zone of fermentation, apparently is influenced by the extent of the zone of fermentation, by the type of carbohydrate, and by the state of health of the intestinal cells.

Effect of Pertussis on the Heart.—LEDBETTER and WHITE (*Jour. Am. Med. Assn.*, 1925, **84**, 1022) remind us that heart disease, as evidenced in particular by valvular deformity, is occasionally found in young people without a history of rheumatic fever, chorea, repeated tonsillitis, scarlet fever or diphtheria, and in whom physical examination fails to show evidence of congenital defects of the heart or blood-vessels. Usually these patients show disease of the mitral or of the aortic valves or both, similar to that found after rheumatic fever or chorea. Even in the absence of a past history of such infections, it is often the custom to diagnose these cases etiologically as rheumatic in type. Sometimes it is possible by close questioning to discover that there was a probable rheumatic infection in childhood, often so mild that it may have been overlooked and diagnosed as growing pains. A mild chorea may have been called nervousness. Badly infected tonsils may be discovered. Even with diligent search there are some unexplained cases. A review of the literature and the expression from a number of pediatrists do not yield proof of endocardial or myocardial damage during or after pertussis. Circulatory failure does not seem to occur during pertussis, though the paroxysms of whooping cough undoubtedly do produce a temporary mechanical strain particularly on the right side of the heart. No evidence of damage to the heart in any case as a result of whooping cough could be found in a study of a series of 232 cases seen in the out-patient department of the Massachusetts General Hospital, and the Children's Hospital, Boston. However, one child had chronic endocarditis and had congenital heart disease before the infection. They were unable to find any evidence that whooping cough has a damaging effect on the heart.

The Ultraviolet Rays of the Sun.—HESS (*Jour. Am. Med. Assn.*, 1925, **84**, 1033) feels that rickets affords an excellent criterion for the investigation of the biologic activity of the rays of the sun, for it is known within narrow limits the band of ultraviolet radiations that is effective in preventing or curing this disorder. A comparison of the yearly amount of actual sunshine in cities in the temperate zone demonstrates that there is no close parallelism between the incidence of rickets and annual sunshine. It shows that the occurrence of rickets does not depend on an equable distribution of sunshine throughout the year. In the Panama Canal Zone, where rickets is practically unknown, not only is the yearly sunshine less than in New York but it is even less evenly distributed. There are fewer hours of sunshine during the rainy season in Panama than during the corresponding winter period in New

York. The determining factor is the quality, not the quantity of the sun's rays. The amount and intensity of the short ultraviolet radiations alone are of value in preventing rickets. The results of heliotherapy during the winter months have been disappointing, owing to the fact that the antirachitic region of the solar spectrum is very limited at this season, and that the infants cannot be exposed directly to the rays of the sun on account of the severity of the climate. It would seem that the amount of the effective solar radiations is so small in winter that even if we substitute quartz panes for ordinary window glass, it will be insufficient to afford protection and eradicate rickets. The most promising therapeutic measures are ultraviolet light from artificial sources or the use of cod liver oil, or potent extracts of this oil.

Irradiated Foods and Irradiated Organic Compounds.—STEENBOCK and DANIELS (*Jour. Am. Med. Assn.*, 1925, **84**, 1093) state that light can impart antirachitic properties to certain compounds, which furnishes the explanation why light acting directly on the body and cod liver oil taken by mouth can have the same action in preventing rickets. When light acts directly on the body, it acts in part by virtue of the fact that it activates antirachitically certain substances already present. Superficially considered, it thus becomes immaterial whether active compounds are ingested or whether they are activated after they are absorbed. The end result is similar. It may stimulate the question why antirachitic activity is not more generally distributed in foods ingested by man and animal, because plant materials can be produced only in the light by photosynthetic activity. This is probably no more peculiar than that rachitis should occur at all, because just as foods are activated by exposure to light, it yields directly to light treatment. The explanation to this is to be found in the fact that solar radiation as it reaches the earth does not carry much of the ultraviolet rays, and it is only light found in this region of the spectrum that is active in this manner. This light has very little penetrating ability, so that plants unprovided as they are with any system for the translocation of lipoids cannot be affected to a high degree. Another question that arises but which is answered with more difficulty is what is going to be the future of irradiated foods and highly purified organic compounds? The answer to this may be anticipated on the basis of what is now known in regard to the effect of light of the proper wave length on various diseases. Of the possibility of their use in rickets, there remains no question, and it is not to be forgotten that rickets is only one form of disturbed calcium relation. By exposing such foods as wheat, rolled oats, corn, hominy, cream of wheat, shredded wheat biscuits, corn flakes, patent wheat flour, cornstarch, meat, milk and egg yolk to ultraviolet light, they can be endowed with antirachitic properties. That such a wide variety of foods can be thus affected appears to be due to the fact that practically all naturally occurring foods contain lipoidal constituents of the nature of sterols which can carry this activation. Cholesterol as obtained from the brain is entirely inactive, but after exposure to ultraviolet light becomes antirachitic. As fats are good solvents for these lipoids, practically all fresh fats such as butter fat, olive oil, lard, corn oil, cocoanut oil and cottonseed oil, can be activated, often to a degree to

make them compare favorably to cod liver oil. As antirachitic action consists in the induction of calcium assimilation and its conservation for the animal, this is a matter that concerns not only the young but also the adult. It is suggested that these findings may have their significance not only in nutrition, but also in the therapy of those diseases known to respond to irradiation with ultraviolet light.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

JOHN H. STOKES, M.D.,

PROFESSOR OF DERMATOLOGY AND SYPHILOLOGY AT THE SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA,

AND

LOREN W. SHAFFER, M.D.,

ASSISTANT PROFESSOR OF DERMATOLOGY AND SYPHILOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA.

Mycotic Paronychia and Dermatitis.—KINGERY and THIENES (*Arch. Dermat. and Syph.*, 1925, **2**, 186) report a new dermatomycosis occurring as an occupational dermatitis known locally as "fruit poisoning," occurring in certain canneries of the Northwest, particularly during the pear canning season. There is a rather marked paronychia characterized by inflammatory reaction, pain, and the actual loss of one or more nails. In addition maceration, vesiculation, and fissuring between and on the interdigital aspects of the fingers are frequently found and occasional patches of erythematovesicular dermatitis of the hands and forearms. Cultures from several patients have uniformly revealed pure cultures of a yeast like organism. Animal and human inoculations result in a clinical picture practically identical with known mycelial infections of the skin and exactly corresponding to the symptoms of patients suffering from the disease. This "fruit poisoning" may then be properly classified with the now known dermatomycoses.

Mouth Lesions of Erythematous Lupus.—CLARK W. FINNERUD (*Arch. f. Dermat. und Syph.*, 1925, **148**, 318) quotes Trautmann as stating that mouth lesions occur in association with erythematous lupus, involving the buccal mucosa in 43 per cent of the cases; the gums, in 32 per cent, and the tongue, in 9 per cent. Finnerud describes a case in which the entire mucous membrane of the mouth was involved with periodic exacerbation, coincident with the use of a preparation known as Krysolgan. The mucosal lesions are raised red or bluish-white patches, often punctiform and linear in outline. The differential diagnosis includes corrosion of the mucous membranes by chemicals, stomatitis, leukoplakia, and the mouth lesions of lichen planus. The process in erythematous lupus shows no necroses, such as occur in

corrosive processes, and the mucous membrane is not diffusely swollen. Stomatitis likewise shows marked swelling and purulent discharge about the niches in the gums, which does not occur in erythematous lupus. The process is differentiated from leukoplakia by the presence of telangiectasis in erythematous lupus with inflammatory changes, which are absent in leukoplakia. The most pronounced leukoplakia is rarely diffuse and the gums are likely to remain free. Central atrophy of the mucosal patches in erythematous lupus may occur, which also distinguishes it from leukoplakia. Epithelial thickening of lichen planus is more sharply defined. There are occasional annular figures and very little inflammatory change. In lichen ruber pemphigoides small erosions may be found. Lichen planus of the mucous membranes presents no subjective symptoms, while burning pain, and dryness of the mouth are the rule with erythematous lupus.

Amyloidosis of the Skin.—H. KÖNIGSTEIN (*Arch. f. Dermat. und Syph.*, 1925, **148**, 330) describes miliary papular amyloidosis of the skin in association with general amyloidosis. The clinical picture consists of small papules and nodules in the skin, most conspicuous about the eyelids, on the forehead, along the vermilion border of the lips, on the palms of the hands, and the dorsums of the feet. The papular and nodular infiltrations about the genitalia are strikingly shown in moulages. Practically no portion of the skin is completely exempt except the dorsal surfaces of the hands and the plantar surfaces of the feet. The patient was a man, sixty years of age, who, following erysipelas of the face, had had pain in the shoulders and extremities for two years, coincidentally with an abundant crop of the hard nodules already described. There were no cutaneous subjective symptoms associated. Somewhat later, erosions on the mucous membranes appeared with intestinal disturbances and cachexia. Atrophy of isolated muscle groups developed. The intestinal picture was associated with symptoms of peritonitis and ileus. In addition to the general miliary papular lesions, larger tumors were found in the fascia and musculature. A diagnosis of amyloid was made histologically, and the postmortem demonstrated the universality of the involvement. A second case is described, and the literature of the condition reviewed. Localized amyloidosis of the skin has been described by Herxheimer, Gutmann, and others. The clinical resemblance to lichen planus is mentioned.

Investigations into the Isolation and Chemical Composition of Trichophytin, the Active Antigenic Principle of Pathogenic Molds.—BR. BLOCH, A. LABOUCHÈRE and FR. SCHAAF (*Arch. f. Dermat. und Syph.*, 1925, **148**, 413). Trichophytin is the substance which can be isolated from pathogenic molds and which gives rise to cutaneous sensitization reactions and, in all probability, to the general allergic or sensitization manifestations produced by these fungi in the patient. Bloch and his collaborators have done an extremely interesting and important work in attempting to isolate the pure substance. While their effort has not been wholly successful as yet, they feel that they can now define trichophytin as a nonprotein substance, which can be dialyzed through a parchment membrane and appears to be in close combination with a water soluble, nitrogen containing polysaccharid.

Its total nitrogen content is approximately 6.75 per cent, amino-nitrogen, 1.3 per cent. The authors are not yet prepared to state that the polysaccharid is the active principle itself but provide in their discussions for the possibility that the nitrogen containing element may be physically bound or absorbed by the polysaccharid. The substance is extremely stable and physiologically active.

Painful Nodular Growth of the Ear.—O. H. FOERSTER (*Arch. Dermat and Syph.*, 1925, **2**, 149) reports 12 cases of this condition, the lesion consisting of a small nodular painful growth on the rim of the ear, usually on the upper pole in the region of the crown angle. The growths are single, ovoid or circular, well defined and firm nodules, varying from 3 to 10 mm. in their longest diameter. They are imbedded in the skin or elevated several millimeters above the surface and usually firmly attached to the cartilage. They often show a central depression and a surrounding zone of hyperemia. Pain is a characteristic feature. It may be quite acute, preventing the patient from resting the head on the affected side or awakening him from sleep. Histologically the lesion presents an inflammatory reaction of unusual diffuseness and depth, intense edema, and degeneration of both collagen and elastic tissue. The etiology is unknown. Excision of the nodule inclusive of the cartilage is the treatment of choice. Roentgen ray and radium usually give relief, but recurrence is frequent.

Experimental Studies on Eczema.—KLAUDER and BROWN (*Arch. Dermat. and Syph.*, 1925, **2**, 283). The purpose of this study was to repeat the experimentation of Luithlen concerning the influence of diet and metabolism of bases with particular reference to the calcium balance in relation to skin sensitivity. Their experiments on rabbits and cats to standardized external irritation showed that the cutaneous irritability was altered by diet, injections of drugs and colloidal substances, by narcosis and experimentally produced nephritis and hepatitis. Such altered cutaneous sensibility could not definitely be correlated with blood chemistry studies and especially the calcium content of the blood. However, they obtained some evidence that metabolism of basic substances, particularly calcium, plays a role in determining altered sensibility of the skin. Rabbits under the influence of a diet rich in albumin will react very much more definitely to irritation than those on green fodder diet, and the animals to which salts of calcium are given acquire a decreased sensibility to irritation of the skin. Their observations would tend to show, however, that other factors are concerned in addition to the metabolism of bases.

On the Treatment of Syphilis of the Aorta.—H. SCHOTTMÜLLER (*Am. Jour. Syph.*, 1925, **9**, 1) is an advocate of intensive treatment of all types of aortitis with arsphenamine and mercury. He makes the radical statement that intensive treatment is always indicated, never harmful. He classifies aortitis as aortitis coronaria, aortitis supracoronaria and aortitis valvularis. Aortitis coronaria is often amenable to treatment. Aortitis supracoronaria affords the most favorable prognosis. Syphilitic insufficiency of the aorta in its early stages is a curable condition so long as cardiac hypertrophy remains the only

physical sign. Aortitis valvularis constitutes the most dangerous form of this affection. A cure from the anatomic point of view can only be expected in the early stages of the disease. He opposes symptomatic treatment and a preparatory period on mercury as a waste of valuable time by withholding arsphenamine treatment. Treatment consists of weekly injections of neoarsphenamine 0.45 to 0.6 gm. for a total of at least 5 gm. followed by a rest interval of two months on potassium iodide. Mercury is given simultaneously either by weekly intramuscular injections of calomel or mercury salicylate or a soluble mercurial intravenously. The patients are then kept continuously under the influence of arsenicals for two to three years, being given an intravenous injection of 0.45 to 0.6 neoarsphenamine every four weeks or repeating the above course twice yearly. This article presents many points of interesting contrast with current views.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Five Cases of Pregnancy with Abdominal Myomectomy.—GOULLIOUD (*Gynéc. et Obst.*, 1924, **9**, 268) reports five cases of myomectomy occurring during pregnancy. The first was in a woman, aged twenty-seven years—a large tumor from the posterior surface of the uterus at the fundus. This was removed before the patient's pregnancy, and the question arose whether from the size of the tumor pregnancy and successful parturition would be possible. The patient made a good recovery, and was told that she might marry. Some years later she had a normal pregnancy followed by spontaneous childbirth, and again suffered from hemorrhage with symptoms of a return of the growth. At this time she was treated by two tubes of radium, 120 mg., for twenty-four hours, followed by the cessation of the hemorrhage and the diminution in size of the tumor. The second patient had an abortion at four months, followed by a spontaneous labor, and at that time it was discovered that she had a fibroid tumor. The tumor was interstitial on the anterior wall and was removed, and the patient had some fever after the operation. Hematoma followed in the right lower quadrant, which simulated appendicitis. She recovered and afterward had an early abortion and then another pregnancy. She entered the hospital for confinement and was successfully delivered of a living child. On her recovery no evidence of fibroid tumor could be found. The third case had an abortion at six months and was found to have a uterine fibroid. Myomectomy was difficult, but was performed and the patient made a good recovery, complicated by a stitch abscess which persisted for some time. She afterward had a spontaneous labor and successful recovery, and six years after the operation

was in good health. In the following year she was found to have a fibroid the size of an orange and the uterus was extirpated. From this she made a good recovery, and on examination the uterus was found to contain many interstitial fibroids. The scar of the first operation was sound and complete healing had occurred. The next patient had an early abortion at two months followed by another at five. There was a uterine fibroid of considerable size and this was removed. Following this there was another abortion, and an effort was made to thoroughly examine the patient, but she passed from observation. A case is cited in which five pregnancies in succession were successful following the removal of a fibroid of considerable size. The removal of a fibroid on the anterior wall and the emptying of ovarian cysts occurred in a patient who had a three months' abortion later. Following this there were signs of return with hemorrhage, and the patient was treated by radium. He reports several cases where the removal of the fibroid was followed by successful pregnancy. One patient had decided not to marry because she had a fibroid tumor of considerable size. She became anemic, and operation was necessary which was successfully carried out and a large tumor removed. The patient, married and gave birth to a deformed child which did not long survive and this was followed later by a spontaneous birth of a healthy living infant. An interesting case is reported in which a patient had a fibroid tumor and also a cyst in which operation was done in early pregnancy, and the pregnancy was not suspected. It was not interrupted and the patient went on to full term, when she entered the hospital with a child in shoulder presentation. This was corrected by external manipulation, but hemorrhage followed and placenta previa was present. A still-born child was delivered by version, and the mother recovered from the labor. A patient, aged thirty-five years, had a myomectomy followed by pregnancy, prolonged labor, application of the forceps and death from septic infection. An extraordinary case is reported in which a patient had a fibroid tumor complicating pregnancy and an abortion. Myomectomy was performed and, on examination, it was thought that the tumor was malignant. The patient recovered and again became pregnant, with placenta previa. On examination it was found that a small fibroid had developed in the broad ligament, which rendered vaginal delivery impossible, and the patient was delivered by section and the uterus extirpated. The child survived the operation, and the mother had a ureteral fistula which required nephrectomy and the opening of an abscess in one of the broad ligaments. She finally, however, made a recovery. From a study of his cases the writer concludes that 25 per cent of women having fibroid tumors of the uterus and exposed to impregnation become pregnant, and that among married women the age of these patients is usually less than forty years. He believes that if women, aged about thirty years, having fibroid tumors of the uterus have these tumors removed successfully they are competent to pass through pregnancy and parturition successfully. The obstetrician may then propose myomectomy to women of a child-bearing age with a good prospect of success. If at operation he found myomectomy to be impossible he can advise hysterectomy or close the abdomen and treat the patient by radium or the

roentgen-ray. In labor following myomectomy there is no special difficulty provided the uterine wound has soundly healed. It must be remembered that most myomectomies are done upon primiparæ beyond the usual age of childbirth, and that in such patients labor is usually prolonged and difficult. One cannot rule out the possibility of small fibroids in the cervix, whose existence may not be detected until operation, and which render the development of pregnancy difficult and spontaneous labor impossible. Malignancy in a fibroid must also be taken into consideration. Patients who have had myomectomies, but have afterward become pregnant, must be cautioned to go to the hospital for confinement, for complications may occur which require surgical help. In some cases fibroid tumors may develop in the uterus as late as ten years after myomectomy. Radium or the roentgen-ray may then be successfully employed to check the growth of such tumors. The next is a curious case of double uterus with fibroma, pregnancy in one half, treated by hysterectomy. DAMBRIN and BERNARDBEIG (*Gynéc. et Obst.*, 1924, **9**, 293) report the extraordinary case of a woman, aged twenty-seven years, whose history was unimportant and who had been married about a year when she sought medical advice. A hematoma in the vulva had developed which suppurated and required opening, and the patient complained of considerable pain. On examination the abdomen was enlarged and painful; there was a sensation of weight in the lower abdomen and a leucorrheal discharge. Menstruation had ceased about three months before; pain had increased; the abdomen had grown in size, and the patient suffered from constipation, nausea and vomiting. On inspection the abdomen contained a globular tumor in the median line, painful on pressure. There were two vaginal openings: The one on the right of normal size and the one on the left small and retracted. On the right side a cervix was found which was that of the pregnant uterus. The right side of the uterus was found enlarged, and the separation of the two vaginæ terminated at the uterine neck. There was a small cervix and tumor on the left side. The patient was in bad general condition, and a diagnosis was made of a small ovarian cyst complicating pregnancy. At operation a double uterus was found with a fibroid on one side and pregnancy on the other. The side containing the fibroid was removed and the side containing the pregnancy was not disturbed. The examination of the tumor removed showed an edematous fibromyoma. The patient recovered from the operation and later gave spontaneous birth after a somewhat prolonged labor to a healthy living child, weighing 2050 gm.; the child was normally developed. The partition between the two vaginæ was removed by the labor. The writer adds a detailed review of this case illustrated by drawings.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,
AND
FRANK B. BLOCK, M.D.,
INSTRUCTOR IN GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Fibroid Tumors of the Vulva.—Fibroid tumors of the vulva are uncommon, although they are the most frequently observed benign solid tumors of this region. In reporting an interesting case of this type, FULLERTON (*Surg., Gynec. and Obst.*, 1925, **40**, 244) presents a nice discussion of the subject which we shall briefly abstract. The tumors occur almost invariably during the child-bearing period, although they do occur later and have been observed in infants. Virgins and parous women seem to be about equally affected. The tumors are usually single and are first seen as small, firm rounded and smooth or slightly lobulated, painless subcutaneous masses. The smaller ones, especially if deep, may easily be overlooked. Pedunculation is common, particularly in the larger tumors. Growth may be rapid, although it is more often slow. Interference with locomotion or discomfort from position send the woman to the surgeon. The skin over the tumor is wrinkled, often more or less pigmented, and freely movable. Because of the increased vascularity of the parts during menstruation and pregnancy, more rapid growth is often noticed at these times. Ulceration is rare, although such a complication occurs from interference with the blood supply or external irritation. Degeneration and malignant transformation are more common in these tumors in this location than in similar tumors located elsewhere in the body, probably because of their variable blood supply, pedunculation and position, which makes trauma more or less unavoidable. Edema, hyalin and cystic degeneration, calcification, ulceration, infection and sarcomatous transformation have all been observed in these tumors. They originate in the connective tissue and may start anywhere in the vulvar structures or in the extraperitoneal portion of the round ligament or internal genitalia, and as they increase in size they are forced into the line of least resistance down the inguinal canal or vagina and appear at the vulva.

Treatment of Pelvic Suppuration.—While we cannot endorse the method of treatment which WORRALL (*Surg., Gynec. and Obst.*, 1925 **40**, 174) employs in cases of pelvic suppurtion, it has given him such satisfactory results in his service in the Sydney Hospital that we present it for those who may be interested. According to his method when there are indications of the presence of pus or any acute, pelvic condition, a preliminary vaginal celiotomy is made, usually posterior to the uterus, into Douglas' pouch, but when the physical signs point to the collection being anterior to the uterus, the bladder is dissected up and the entry made into the uterovesical pouch. The

pus is evacuated, the pus sacs are defined and punctured, and a large split rubber tube is inserted and stitched in the opening. The tube is split in order to lessen the danger of pressure necrosis of the inflamed, softened bowel. Iodoform gauze is sometimes used in addition, but never passed into the tube. In forty-eight hours after this operation the constitutional symptoms have usually undergone a great improvement, and at the end of a week, or perhaps a few days more, the patient having eliminated the toxins, feels well. She then undergoes the second stage of the operation. After removal of the gauze and the tube, the drainage tract and vagina are cleansed with 25 per cent hydrogen peroxide, and abdominal section is performed, the suppurating focus removed and a fresh drain placed through the vagina. Under this plan of treatment all acute pelvic conditions, except the first attack of a mild gonorrheal salpingitis, are operated upon without delay; if the patient is very ill, on the day of admission. "Waiting for the temperature to settle down and the pus to lose its infectivity" has not been practised. Should one fail to evacuate pus by the vaginal incision, abdominal section is performed at the same sitting, the offending focus removed and vaginal drainage established. The writer states that he always practises vaginal celiotomy preliminary to abdominal section, when there is reason to anticipate a considerable number of adhesions or unusual difficulties from past infection. Iodoform gauze is passed into the wound in the vaginal vault, and this is a landmark in carrying out the removal of the focus from above. When the writer presented this paper before the American College of Surgeons the American gynecologists who discussed it were unanimously opposed to the procedure.

Importance of Urethral Prolapse in Women.—On account of the frequency of confusion in diagnosis between urethral caruncle and urethral prolapse in women, and especially on account of the importance of the latter condition as a symptom of disease higher in the urinary tract, CHUTE (*Boston Med. and Surg. Jour.*, 1925, **192**, 162) reminds us that the term urethral caruncle should be limited to the little raspberry-like growths that are seen at the meatus. They are true papillomas of the urethra and produce stinging on urination, occasionally a little urethral bleeding and sometimes even a little urethral discharge. They rarely produce marked symptoms of bladder irritation or any considerable amount of bleeding. He cites three cases which had previously been operated upon for "urethral caruncles" but later developed bladder tumors, and he is of the opinion that the so called caruncles were probably cases of prolapse of the urethra due to vesical straining. The point which he desires to emphasize is that we should be very cautious in accounting for marked urinary symptoms in women as due to the presence of a relatively minor urinary lesion at the meatus. Cases of this sort should be subjected to careful cystoscopic examination before any operation is performed. In cases where the basic trouble is a self-limited inflammatory lesion of the bladder the patient will often improve so much during the convalescence following the operation for the removal of the urethral lesion as to make it seem probable that the relief depended upon the operation, but in cases where the bladder lesion is a serious one, such as a tumor, valuable time will be lost.

RADIOLOGY

UNDER THE CHARGE OF

RUSSELL D. CARMAN, M.D.,

HEAD OF THE SECTION OF ROENTGENOLOGY, MAYO CLINIC, ROCHESTER, MINN.

A Summary of the Effects of Repeated Roentgen-ray Exposures upon the Human Skin, Antecedent to the Formation of Carcinoma.—S. B. WOLBACH (*Am. Jour. Roentgenol. and Rad. Ther.*, 1925, **13**, 139) describes the earliest histological changes found in the skin of guinea pigs and rats as early as forty-eight to seventy-two hours after experimental exposure to roentgen rays, and a striking swelling of the collagen fibrils of the corium, subcutaneous tissue, and the walls of bloodvessels. The epidermis shows no change until the swelling of the collagen fibrils has occurred. The lesions of the epidermis appear to be secondary to the obliteration of the lymphatics and capillaries, caused by the swollen collagen. The maximum effect of radiation is upon the superficial layers of the corium. The initial change appears to be a focus of localized edema immediately below the epidermis separating the epidermis from the viable corium and later a necrosis. The gap is covered by regeneration of the epidermis which becomes altered and migrates downward because of incomplete nutrition. This effect is noted by a thickening and keratinization of the epidermis. This proliferative activity of the epidermis greatly in excess of normal proliferation may be an outstanding fact in the origin of epidermoid carcinoma in chronic roentgen-ray dermatitis. The acquisition of malignant properties is not of sudden onset but acquired in the course of years.

The Normal Movements of the Stomach.—In reviewing the literature, MCCRAE, MCSWINEY, MORISON and STOPFORD (*Brit. Jour. Rad.*, 1925, **30**, 48) found a great diversity of opinion in regard to the normal movements of the stomach. There are two main schools: the first believes that the typical gastric movement consists of two distinct phases: (*a*) Peristaltic wave which involves the body of the stomach and preantral region; (*b*) a contraction of the musculature of the pyloric antrum as a whole. The second school believes that the peristaltic wave sweeps from its origin on the body of the stomach to the pylorus and does not partition the stomach. Cole attempts to correlate the two schools and classifies the different types of peristalsis under the headings of: (*a*) One cycle; (*b*) one-and-a-half cycle; (*c*) two-cycle; (*d*) three- and four-cycle; (*e*) choreic type. The authors examined rabbits, cats and dogs by direct observation under anesthesia and by roentgen-ray examination. The human was studied only by roentgen-ray examination. This work confirms the existence of two distinct types of movement which correspond closely to that described by the two schools. They have in addition observed in a few cases a third variety in which the shallow waves pass on over the formed antrum and is regarded as occupying an intermediate position between the other two types. The

results obtained by direct examination have in great part been substantiated by roentgen-ray findings. The authors believe it probable that the type of movement present is to some extent governed by: (1) The consistency and type of food; (2) the degree of tension of the wall of the organ; (3) the muscular formation of the stomach wall. Their conclusions are as follows: (1) The form of movement known as the two-phase type is that most frequently found in the stomach of man, the dog, and the rabbit; (2) the form of movement known as the one-phase type, or some modification of this, is normally found in the stomach of the cat; (3) either form of movement may on occasion be observed in the stomach of man, the cat, and the rabbit; (4) the movements of the corpus ventriculi and of the pars pylorica may occur with differing rhythms.

Light Treatment in Medicine.—Axel Reyn (*Radiology*, 1925, **4**, 288). In addition to the visible rays in white sunlight there are some invisible ones, the ultraviolet and the infra-red; the ultraviolet have a chemical effect and certain biologic effects on the living organism. In accordance with Finsen's ideas, light is concentrated through lenses for local treatment, and nonconcentrated for exposing the whole body to light baths. For local treatment Finsen used the carbon arc light exclusively for it contains far more ultraviolet rays than sunlight, the ultraviolet rays of which are absorbed by the atmosphere. The installation used for local treatment consists of a 50-ampère carbon arc lamp; hanging around this are four convergent lenses for concentrating the light. The lenses are made of rock crystal, which, unlike ordinary glass, does not absorb ultraviolet rays. For absorption of the heat rays, a layer of water is placed between some of the lenses. In order to prevent absorption of the chemical rays by blood the skin must be made bloodless. This is done by compressing apparatus, by means of which blood is pressed away from the spot to be irradiated. Marked success has been obtained in the treatment of lupus vulgaris, 60 to 70 per cent of permanent cures resulting. Acne vulgaris et roseacea, alopecia areata, roentgen ulcer, xanthelasma and trachoma have also been treated in this manner with varying grades of success. For light baths artificial light must replace sun light in Northern countries, and for this purpose carbon arc lamps are used, with direct current. Hasselback pointed out that skin erythema brought about a fall of blood pressure in the bloodvessels in the periphery and caused deeper inspiration. Therefore, he believed in the light bath treatment of heart disease. Its greatest value is, however, in the various forms of tuberculosis. Often lupus vulgaris has to be treated with light baths in addition to local treatment. Out of 114 cases, 96 were cured by the author by the combination of local treatment and light baths. The results obtained in the treatment of cases of surgical tuberculosis by carbon-arc-light baths "are most astonishing." In tuberculosis of the elbow, for example, 93 per cent cures were obtained. In tuberculous glands, 95 per cent of 500 cases have been cured. Great benefit was also obtained in rhinolaryngologic tuberculosis. The effect of light on tuberculosis cannot be definitely explained. There have been many explanations but the author classes them as merely hypotheses. Nontuberculous diseases are also treated by light baths, among them being hypertension, neurasthenia, simple anemia and rickets.

Radiographic Diagnosis of Periapical Dental Infection.—Cultures were made of the periapical tissues of 1307 vital and pulpless teeth, and the findings compared with the radiographs by RUSSELL L. HADEN (*Radiology*, 1925, **4**, 337). Of 392 vital teeth 9 per cent showed from 1 to 10 colonies in a deep agar tube, 5 per cent 10 or more colonies and only 1 per cent over 100 colonies. Ten per cent of 490 pulpless teeth negative in the radiograph, showed from one to 10 colonies, 44 per cent had 10 or more and 24 per cent had over 100 colonies. Of 425 pulpless teeth with positive radiograph, 10 per cent showed from 1 to 10 colonies, 60 per cent 10 or more and 44 per cent had over 100 colonies. The incidence of infection is almost as high in the radiographic negative group as in the radiographic positive one. There is a very sharp limitation to the translation of radiographic evidence of infection into terms of bacteria. The absence of radiographic evidence of infection at the apex of a pulpless tooth never excludes the presence of active infection. In many cases the radiographic negative tooth is a far greater source of systemic infection than the radiographic positive tooth, since in the former there may be little resistance to infection.

The Treatment of Tuberculosis of the Female Genitalia with Light and Rays.—HENRY SCHMITZ (*Radiology*, 1925, **4**, 283) states that genito-urinary tuberculosis of the female is a local manifestation of a generalized tuberculosis, usually secondary to primary disease in the respiratory or digestive tract. Treatment therefore must be directed toward the disease and not merely toward a local manifestation. The methods of treatment are medical and surgical, each with a curability of 33 per cent, and actinic. The last method consists in the daily application of a light bath of an hour's duration from an Edison carbon light diffused by a reflector. The anterior and posterior body surfaces are each exposed for one-half hour. This is followed by the application of the ultraviolet ray obtained from an air-cooled quartz light, according to Rollier's method. The head is always covered. The body is divided into five parts. A table is given showing the time duration and fields, the time being increased until exposure of fifteen minutes are given daily over anterior and posterior surfaces. A pronounced tanning is produced. Treatment is given every other day, and twice a week for an entire year when local healing has been obtained. If necessary, Roentgen-ray therapy is added to the ultraviolet-ray treatment. If after the second roentgen-ray treatment the general and local condition is not markedly improved, the case is considered refractory to actinic therapy. This does not interfere with surgical procedures that might be indicated. General treatment also must not be neglected. Two case reports are given.

Pneumonokoniosis in the Ruhr.—Twelve cases of pneumonokoniosis with roentgenograms are reported by A. BOHME (*Fortschr. a. d. Geb. d. Roent.*, 1925, **33**, 39). Three were in coal miners and 9 in stone masons. As depicted in the roentgenogram the extent and localization of the process varied among the different cases. In 3 the lateral portions of the lungs were chiefly affected; several had marked involvement of the apices. In most cases the lowermost portions of the lungs were spared. Tuberculosis was a complicating factor in 3 cases.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ., M.D., C.M.,

PROFESSOR OF PATHOLOGY, UNIVERSITY OF TORONTO; TORONTO, CANADA,

AND

W. L. HOLMAN, M.D.,

ASSISTANT PROFESSOR OF BACTERIOLOGY, UNIVERSITY OF TORONTO, TORONTO, CANADA.

Experimental High Intestinal Obstruction in the Monkey.—In previous papers HADEN and ORR (*Jour. Exper. Med.*, 1925, **41**, 107) have reported the essential changes, as they have found them in the blood and urine of man and dog in intestinal obstruction as a primary fall in blood chlorides, usually a rise in alkali reserve, and finally a rise in non-protein nitrogen. The chemical and clinical evidences of toxemia do not appear until the chlorides are well depleted. This paper deals with experimental high intestinal obstruction, aseptically performed, in 5 monkeys. The obstruction was obtained by section and inversion of the cut ends, and an autopsy was always performed to rule out peritonitis. Observations on the blood were made twenty-four hours before operation and at twenty-four-hourly intervals thereafter until death. For purposes of comparison they present the blood chemistry findings in 13 normal monkeys. These findings vary very little from the average normal in man. No vomiting was observed in the experimental animals, though there was a marked fall in blood chlorides in 2 of the monkeys and a less marked but definite fall in the chlorides of the other three. This emphasizes the fact that vomiting alone does not account for the fall in blood chlorides characteristic of intestinal obstruction. All animals showed a marked rise in non-protein nitrogen and coincident with the fall in blood chlorides there was a rise in CO_2 combining power. The uric acid and creatinine showed no typical changes. In a further study of the chlorides, *The Distribution of the Chlorides in the Blood of the Dog after Experimental Intestinal Obstruction* (*Jour. Exper. Med.*, 1925, **41**, 113), the same authors determined the chlorides simultaneously in whole blood in plasma and in the cells, using the van Slyke method. Four animals were used and they all showed the characteristic fall in blood chlorides, this decrease being shown more characteristically in whole blood than in cells or plasma. (The idea of using whole blood in chloride determinations by an ashing procedure is a comparatively recent one of van Slyke's.) It is shown that the fall in chlorides is born almost equally by the cells and the plasma, and that the estimation on whole blood is more desirable than on plasma. It is also demonstrated that the disappeared chlorides do not exist in the blood in some undetermined form and that they must be sought for elsewhere. The findings were compared with those obtained by the iodometric titration on protein-free filtrate and were found to check very closely. Following this, HADEN and ORR (*Jour. Exper. Med.*, 1925, **41**, 119) reported further on the same subject in *The Sodium Content of the Blood of the Dog after Experimental Intestinal Obstruction.* They wished to determine

if possible whether the sodium freed from combination with the chloride is recombined in the form of carbonate, is lost from the blood, remains free or is combined in some other manner. Ten animals were used, and the methods followed were the same as those previously reported (*vide supra*). All animals showed the characteristic rise of non-protein nitrogen, and the CO_2 combining was always increased. Relatively little change in the sodium content was found however. It tended to rise rather than fall. The findings do not support the theory that the increased destruction of body tissues is due to accelerated autolysis following the withdrawal of sodium from body protein. The experiment shows that the loss of acid radicles is not accompanied by a loss of basic, and the manner in which the excess of basic is combined was not determined. No light was thrown on the mechanism of the increased protein destruction characteristic of intestinal obstruction.

Encephalitozoön Cuniculi as a Kidney Parasite in the Rabbit.—The importance of the study of the Encephalitozoön cuniculi (so called "Cameron body") is emphasized by SMITH and FLORENCE (*Jour. Exper. Med.*, 1925, **41**, 25). In reviewing the literature they find that the parasite has been described by Wright and Craighead in the central nervous system, kidneys and urine of rabbits suffering from motor paralysis; by Levaditi, Nicolau and Schwen in the central nervous systems of rabbits used by them in a comparative study of the virus of encephalitis obtained from four different sources, and later in the kidneys of 3 rabbits inoculated with virus from a spontaneous case; by Doer and Zdansky in the brains of 8 out of 224 rabbits. Kling and later Oliver also reported it in rabbits' brains, and recently Goodpasture has described it in the brains and kidneys of rabbits suffering from spontaneous encephalitis. (Reviewed by Da Fano in *Medical Science*, 1923, **10**, 355.) The authors describe the parasite in 45 out of 163 rabbits autopsied. The disease appears to be endemic with an increase in the number of cases in the early summer. It was found in young rabbits only. No characteristic symptoms were presented. When recovered from the kidneys the parasites appear as pale or more highly refractive bodies of rod-like outline 2.5 to 3 mm. long and 1.5 to 2 mm. broad, somewhat Gram-positive and non-acid fast. They occur in dense groups within epithelial cells or singly in the débris in affected tubules. The parasite has the appearance of two coccoid end forms with a slender connection between roughly the form of a figure eight. Variations in the morphology are described. The collecting tubules near the tip of the papilla seem to be the most consistently invaded. The authors offer evidence for and against the status of the organisms as a bacterium or a protozoön, with the balance in favor of the protozoön, and they go on to offer a tentative life cycle. The parasite has been developed in the mouse and the dog. The pathology of the condition insofar as it is at present known seems to be a mechanical blocking of the normal flow of urine from the convoluted tubules and the descending limbs of Henle's loops, leading to dilatation and ultimate cellular reactions. Lymphoid-cell infiltration was noted in the kidney cortex. Lymphocytic filtration was found in various portions of the brain, but localization in the brain

could not be correlated with the cellular reaction. The kidneys are looked upon as the normal habitat of the parasite, while the brain is outside the normal cycle. The authors indicate many attractive ways in which the problem may be further studied.

The Serological Classification of the Tubercle Bacilli by Agglutination and Absorption of Agglutinins.—A series of experiments on the agglutination reaction and the absorption of agglutinins was conducted by G. S. WILSON, University of Manchester (*Jour. Path. and Bacteriol.*, 1925, **28**, 69) to ascertain whether serological differences could be substantiated between the human and the bovine types of tubercle bacilli, whether the human bacilli could be subdivided into serological classes and whether these tests differentiate human and bovine types from other acid-fast bacteria. The investigations were carried out with eighty-nine strains of avian, bovine, human, reptilian and saprophytic acid-fast bacilli, the strain being collected from a great variety of sources. The results of the agglutination tests showed that there was a considerable amount of cross agglutination in the case of every serum, although the avian type showed a fair degree of specificity. With the human and bovine types, however, the specificity was so slight as to be valueless. As it became clear that there was but little differentiation in the direct agglutination test, attention was given to the absorption of agglutinins. The series of experiments showed that the bovine and human strains are indistinguishable serologically. Furthermore, no evidence was found of a multiplicity of types among the human strains tested. The authors concluded, on the basis of the absorption test, that the human type is a homogeneous one and that the bovine and human strains possess a fundamental identity of structure. The investigation showed incidentally that certain well-known strains of tubercle bacilli are masquerading under a wrong denomination. Such a strain as the Koch-Nathan raw strain (the same as the H34 of the author's collection) has been shown to be not a human but an avian strain.

A Peculiar Staining Reaction in Red Blood Cells.—ECKSTEIN (*Virchow's Arch. f. path. Anat.*, 1924, **249**, 118) found that by using the Alzheimer methylene-blue-eosin method of staining that the erythrocytes ordinarily stain red. He observed, however, in other instances, particularly in areas of hyperemia and hemorrhage that the staining reaction was variable, some of the cells being red, others blue. Various gradations between these colors were commonly seen. He has been able to show that the red blood cells when free of carbon dioxide stain red, but when an appreciable amount of carbon dioxide was present at the time of fixation the reaction is blue. This reaction gave satisfactory results, even when the hemoglobin was reduced or when other gases had been absorbed. This finding may explain the reason for the variable staining qualities exhibited by red blood cells in tissues which have been sectioned.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Rocky Mountain Spotted Fever: Experimental Studies on Tick Virus.—SPENDER and PARKER (*Pub. Health Rep.*, 1924, **39**, 3027–3040) review the considerations relative to the natural evolution of Rocky Mountain spotted fever as follows: (1) The disease is maintained in rodents and ticks; human cases are secondary and accidental. (2) The disease exists in definite foci, and the virulence of the infection may vary decidedly even in adjacent areas. (3) A large number of rodent species are susceptible, but there is no evidence that the infection is highly fatal among them. (4) The complete life cycle of the tick includes four stages, and the infection may pass from stage to stage and from one generation to the next. (5) A disintegration of tissue (histolysis) takes place during the premolting period of larvæ and nymphs. (6) The tick ingests mammalian blood three times during the cycle—twice from small rodents (most of them susceptible to spotted fever) as larvæ and nymphs and once from large animals (all immune as far as known except that some adults feed on jack rabbit, snowshoe rabbits, and porcupines, of which animals at least the first two are susceptible to spotted fever) as adults. (7) The virus passes through the egg and larval stages of the tick in one summer, but in the unfed nymphs and adults it has been compelled to adapt itself to the hibernation (also estivation in the adult) which these stages undergo.

The results of the new work is summarized by the authors as follows: (1) In confirmation of earlier observations of previous workers, ticks of the species D. andersoni which have received the infection of Rocky Mountain spotted fever in the larval or nymphal stage retain it in the adult stage. (2) A twenty-four hour incubation at 37° C. of unfed hibernating nymphs and adults infected as larvæ and subsequent injection of emulsions of such ticks into guinea pigs give a higher percentage of positive infection than the injection of similar ticks not incubated. (3) Infection of Rocky Mountain spotted fever in adult ticks subjected to winter temperatures (32° F. or below) may be demonstrated by the production of immunity in guinea pigs following the injection of tick viscera immediately upon removal from cold temperatures, by a moderate but typical spotted fever following the injection of ticks after twenty-four hours incubation at 37° C., and by virulent spotted fever following tick feeding or the injection of ticks after feeding. (4) Control adult ticks free from all infection do not produce death or

illness in guinea pigs by feeding nor by injection of such ticks after feeding. (5) One infected adult tick may contain after feeding, from 3000 to 5000 M. L. D. for a guinea pig. (6) Emulsion of infected fed adult ticks treated with 0.5 per cent phenol will protect guinea pigs against 1 cc of blood virus. (7) Nothing in the behavior of blood or tissue virus is comparable to the changes observed in tick virus.

State-wide Milk Sanitation Program.—FRANK (*Pub. Health Rep.*, 1924, **39**, 2765–2777) states that most municipalities fail to take the necessary steps to safeguard milk supplies unless guided by the State health organization. He considers milk as second only to water in the transmission of disease and lays emphasis on the need for its sanitary supervision. The steps taken in Alabama to reach the desired end were (1) To develop an effective type of milk legislation. (2) To encourage the cities of Alabama to enact it. (3) To insure its effective enforcement; and (4) to measure its results. Safe milk is defined as high-grade milk, pasteurized. The details of the means of providing a safe supply are given.

Diabetes Mellitus. A Contribution to its Epidemiology Based Chiefly on Mortality Statistics.—EMERSON and LARIMORE (*Arch. Int. Med.*, 1924, **34**, 585) state that the increase in the incidence and death rate from diabetes in the United States, and in New York City in particular, has been more rapid than that of any other disease for which we have records in the last fifty years. This increase, while it has affected all ages to some degree, has been most marked among women at all ages and among both men and women over thirty-five years of age in particular. There are wide variations in the susceptibility to diabetes, or at least in their ability to survive when it develops in them, among persons of different races, those of Semitic stock showing consistently the highest death rates and those of the Negro race in the United States the lowest. It is not at all clear that these marked differences in the death rates from diabetes in the people of various races are of fundamental biologic significance, since many elements of occupation, economic status, dietetic habits, and so forth, may be found sufficient to explain the range of experience with what may fairly be considered a disease of a fatigued function in the great majority of cases. Although the relative rarity of diabetes among rural workers and those engaged in hard manual labor or trades would appear significant, the lack of a thoroughly satisfactory basis for calculating death rates by occupational groups in this country deprives the contrasting picture, of high rates among desk workers and others engaged chiefly in mental rather than physical processes for their living, of much of its force. Seasonal variations in death rates, calculated on a monthly basis, are marked and apparently significant. Whether temperature and other accompanying weather conditions are responsible, or the similar seasonal incidence of infections, usually accompanied by fever and interference with nutrition and deteriorated bodily resistance, cannot be stated on the basis of present information. Geographical distribution of the disease as measured by death rates in the United States appears to be explicable on the basis of differences in the age grouping, race, economic status, and occupation of the people, high rates being found where there is a

high proportion of the population in the later decades of life, after forty-five, where there are many Jews and where per capita wealth is high. Where life expectancy is high, there is a lower diabetes death rates than in states where life expectancy is low, but this is probable due to the fact that the low expectancy states are those with a high proportion of Negroes in the population. The changes in food habits in the United States have probably contributed to the increase of diabetes, the higher carbohydrate element and greater abundance or superalimentation being believed to be a cause of overfatiguing the function of sugar tolerance. It is considered of much importance that educational measures be instituted to inform the public through medical and public health channels of the seriousness of the situation, and of the necessity of adjustment of food intake to exercise and *vice versa*. Moderation in the use of food and sufficient exercise with the entire body to justify the food absorbed, are important rules of hygiene for other reasons besides that of the relationship between obesity and diabetes, but if there were no other excuse for bringing this ancient teaching to people's attention, the greatly increased frequency of diabetes as a cause of sickness and death would alone seem to justify physicians and all those dealing with health and its protection in initiating and pushing vigorously a campaign of information in this subject.

The Seasonal Prevalence of Infantile Paralysis. Seasonal Variation in Case Fatality Rate.—Aycock and Eaton (*Am. Jour. Hyg.*, 1924, **4**, 681) state that there is a marked seasonal variation in the ratio of reported morbidity to reported mortality of infantile paralysis. This variation, in their opinion, is due largely to failure to recognize the milder forms of the disease in its "off season" and to a lesser extent to delayed reporting of cases as against prompt reporting of deaths. According to a calculated seasonal morbidity on the basis of the observations, infantile paralysis, although preponderantly a summer disease, prevails to a greater extent in the season from December to May than is shown by the reporting of cases. A calculated morbidity for 1921 also shows a secondary increase in the prevalence of the disease in March, which was not shown in the reporting of cases.

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